

Fig. 1A-1

Sequence	2105	KM643-4-11	F2-103	110	KM341-1-19
1. EPPTACREKQYLI	16353	13220	31427	13403	14108
2. PTACREKQYLINS	17358	13220	39202	13575	14194
3. ACREKQYLINSQC	20267	13212	35911	13681	14013
4. REKQYLINSQCCS	17096	13305	43762	13685	13952
5. KQYLINSQCCSLC	23249	13292	36839	13894	13779
6. YLINSQCCSLCQP	16140	13470	44975	13964	13909
7. INSQCCSLCQPGQ	15918	13390	54811	13652	13751
8. SQCCSLCQPGQKL	18804	13271	60441	13872	13819
9. CCSLCQPGQKLVS	16534	13436	56601	13821	13851
10. SLCQPGQKLVSDC	18155	13314	54718	13705	13965
11. CQPGQKLVSDCTE	17614	13460	52073	13699	13781
12. PGQKLVSDCTEFT	91270	13334	58177	13464	13725
13. QKLVSDCTEFTET	96926	13465	49003	14916	13875
14. LVSDCTEFTETEC	141877	13634	62580	13394	13783
15. SDCTEFTETECPL	148692	13213	42916	13571	13696
16. CTEFTETECPLCG	145926	13591	38170	13220	13824
17. EFTETECPLCGES	136350	13593	56597	13434	13638
18. TETECPLCGESEF	77805	13298	33201	13398	13723
19. TECLPCGESEFLD	50648	13544	29781	13488	13685
20. CLPCGESEFLDTW	79246	13736	26075	13599	13807
21. PCGESEFLDTWNR	93482	13626	44337	16142	13830
22. GESEFLDTWNRET	68932	14815	45811	13777	13832
23. SEFLDTWNRETHC	105899	13777	40462	14023	13898
24. FLDTWNRETHCHQ	55803	15498	79990	40210	13937
25. DTWNRETHCHQHK	19237	13367	34525	13995	13737
26. WNRETHCHQHXYC	22963	13843	32912	15601	13595
27. RETHCHQHXYCDP	16522	13282	41600	13644	13595
28. THCHQHXYCDPNL	25181	13211	32264	13567	13621
29. CHQHXYCDPNLGL	16455	13300	34480	13684	13671
30. QHXYCDPNLGLRV	16627	13541	39057	13461	13670
31. KYCDPNLGLRVQQ	16429	13491	46485	13452	13779
32. CDPNLGLRVQQKG	16877	13454	90926	13293	13799
33. PNLGLRVQQKGTS	18117	13611	123330	13358	13917
34. LGLRVQQKGTSSET	22898	13512	237353	13381	15032
35. LRVQQKGTSSETDT	24787	13599	250401	13364	13774
36. VQQKGTSSETDTIC	28492	13372	35303	13124	13686
37. QKGTSSETDTICTC	27724	13490	35334	13298	13569
38. GTSETDTICTCEE	18834	13340	29905	13289	13525
39. SETDTICTCEEGW	16914	13340	24871	13315	13486
40. TDTICTCEEGWHC	17866	13568	24475	13481	13631

Fig. 1A-2

Sequence	2105	KM643-4-11	F2-103	110	KM341-1-19
41. TICTCEEGWHCTS	18122	13767	24169	13564	68670
42. CTCEEGWHCTSEA	17485	18955	28190	13736	75214
43. CEEGWHCTSEACE	16859	41843	32056	13525	16033
44. EGWHCTSEACESC	17735	13381	35518	13771	13867
45. WHCTSEACESCVL	64890	13444	38190	13708	13687
46. CTSEACESCVLHR	16788	13446	39497	13859	13636
47. SEACESCVLHRSC	16421	13555	40206	13482	13584
48. ACESCVLHRSCSP	15795	13183	36735	13503	13575
49. ESCVLHRSCSPGF	47038	13504	41251	14500	13637
50. CVLHRSCSPGFGV	17469	13279	45795	13484	13573
51. LHRSCSPGFGVKQ	16635	13382	88644	13187	13567
52. RSCSPGFGVKQIA	16642	13339	114128	13368	13623
53. CSPGFGVKQIATG	17457	13485	110624	13323	13703
54. PGFGVKQIATGVS	18818	13577	253876	13234	13769
55. FGVKQIATGVSDT	20521	13429	697242	13178	13903
56. VKQIATGVSDTIC	20855	13510	91544	13176	13681
57. QIATGVSDTICEP	19014	13523	40193	13154	13575
58. ATGVSDTICEPCP	17139	13526	38012	13127	13599
59. GVSDTICEPCPVG	16515	13508	31118	13376	13571
60. SDTICEPCPVGFF	42762	13590	25542	13392	13534
61. TICEPCPVGFFSN	25039	13366	27921	13524	13783
62. CEPCPVGFFSNVS	18141	13429	31377	14364	13717
63. PCPVGFFSNVSSA	20806	13343	51411	19243	13979
64. PVGFFSNVSSAFE	95541	14553	128669	158203	14523
65. GFFSNVSSAFEKC	67908	13506	94016	14323	13831
66. FSNVSSAFEKCHP	22379	13350	124184	14057	13699
67. NVSSAFEKCHPWT	18703	13298	44966	13518	13676
68. SSAFEKCHPWTSC	19809	13459	37784	13433	13553
69. AFEKCHPWTSCET	16212	13387	38013	13279	13683
70. EKCHPWTSCETKD	15198	13423	39248	13315	13494
71. CHPWTSCETKDLV	15754	13383	40627	13228	13673
72. PWTSCETKDLVVQ	15609	13426	46662	13247	13613
73. TSCETKDLVVQQA	16454	13377	46750	13228	13670
74. CETKDLVVQQAGT	16875	13544	42504	13185	13700
75. TKDLVVQQAGTNK	17357	14026	83860	13184	13674
76. DLVVQQAGTNKTD	17735	13434	34853	13154	13776
77. VVQQAGTNKTDVV	17176	13805	51573	13166	13651
78. QQAGTNKTDVVCG	15794	13261	27337	13103	13398
79. AGTNKTDVVCGPQ	15793	13448	25989	13304	13658
80. TNKTDVVCGPQDR	15114	13481	24807	13199	13767
81. KTDVVCGPQDRLR	15782	13328	35951	13548	14112
82. DVVCGPQDRLRAL	16644	13255	33393	13756	14104

Fig. 1B-1

Sequence	F4-465	281-1-10	2B11	F72	F76	4D11
1. EPPTACREKQYLI	20561	4194	14158	3965	3348	14138
2. PTACREKQYLINS	19249	4141	14276	3906	3420	14387
3. ACREKQYLINSQC	20418	4221	14276	3884	3300	14044
4. REKQYLINSQCCS	20278	4080	14214	3849	3546	13956
5. KQYLINSQCCSLC	19642	4169	14082	3806	3378	14443
6. YLINSQCCSLCQP	19658	4184	14231	4082	3464	14432
7. INSQCCSLCQPGQ	18482	4603	13927	3986	3157	13783
8. SQCCSLCQPGQKL	19075	4326	13748	3934	3675	13471
9. CCSLCQPGQKLVS	20282	4349	13578	4046	3336	13431
10. SLCQPGQKLVSDC	20175	4841	13522	3948	3222	13387
11. CQPGQKLVSDCTE	22520	4576	13441	4115	3566	13339
12. PGQKLVSDCTEFT	23688	4499	13618	4012	3525	13290
13. QKLVSDCTEFTET	22029	4771	13528	4294	3539	13450
14. LVSDCTEFTETEC	23692	5212	13439	4177	3601	14898
15. SDCTEFTETECPL	25950	4864	13359	4095	3362	13277
16. CTETETETECPCG	20943	4906	13496	4121	3582	13874
17. EFTETETECPCGES	37123	4748	13570	3960	3402	16583
18. TETETECPCGESEF	23400	4807	13444	3811	3407	13808
19. TECLPCGESEFLD	21427	4649	13352	3970	3288	13566
20. CLPCGESEFLDTW	18021	4794	19449	3940	5926	47209
21. PCGESEFLDTWNR	26480	7656	86887	5478	16438	165895
22. GESEFLDTWNRET	25229	4906	24124	4337	4362	32083
23. SEFLDTWNRETHC	23274	5979	30344	4138	4083	72724
24. FLDTWNRETHCHQ	28280	19544	120439	4636	6401	336496
25. DTWNRETHCHQH	20114	4107	14285	4029	3459	14028
26. WNRETHCHQHXYC	21110	4714	16070	4111	3819	25715
27. RETHCHQHXYCDP	19452	4075	13942	4000	3252	13812
28. THCHQHXYCDPNL	18412	4221	14203	3912	3459	14295
29. CHQHXYCDPNLGL	18890	4288	16566	4025	3473	13886
30. QHXYCDPNLGLRV	19296	4313	13580	4132	3383	13355
31. KYCDPNLGLRVQQ	20430	4460	13469	4254	3651	13357
32. CDPNLGLRVQQKG	28700	4570	13568	5394	4575	13336
33. PNLGLRVQQKGTS	39822	5229	13590	24278	6996	13404
34. LGLRVQQKGTSSET	52908	4681	13651	7042	4112	13400
35. LRVQQKGTSSETDT	56985	4376	13514	4839	16679	13557
36. VQQKGTSSETDTIC	21684	4531	13423	3960	3258	13355
37. QKGTSSETDTICTC	21838	4509	13507	3975	3355	13365
38. GTSETDTICTCEE	21896	4074	13348	3856	3298	13453
39. SETDTICTCEEGW	18789	4082	13377	3687	3297	13606
40. TDTICTCEEGWHC	17729	4187	13485	3756	3638	19679

Fig. 1B-2

Sequence	F4-465	281-1-10	2B11	F72	F76	4D11
41. TICTCEEGWHCTS	22932	4207	14559	4151	3992	46128
42. CTCEEGWHCTSEA	22823	4167	14428	4077	3394	14309
43. CEEGWHCTSEACE	25545	4071	14192	4118	3375	14162
44. EGWHCTSEACESC	23461	4272	14290	4171	3393	14029
45. WHCTSEACESCVL	20999	4198	14136	4318	3465	14065
46. CTSEACESCVLHR	20553	4273	14301	4152	3396	14337
47. SEACESCVLHRSC	20792	4234	13900	4122	3439	13877
48. ACESCVLHRSCSP	21816	4179	13741	3934	3525	13539
49. ESCVLHRSCSPGF	20599	4725	13758	4141	3514	13658
50. CVLHRSCSPGFGV	19851	4393	13533	4127	3526	13320
51. LHRSCSPGFGVKQ	23160	4317	13486	4851	18376	13355
52. RSCSPGFGVKQIA	24797	4495	13728	5568	15564	13375
53. CSPGFGVKQIATG	30890	4962	13400	8711	3383	13340
54. PGFGVKQIATGVS	82448	5027	13415	11404	4102	13378
55. FGVKQIATGVSDT	126309	4541	13423	4896	3515	13474
56. VKQIATGVSDTIC	32389	4361	13454	4040	3278	13305
57. QIATGVSDTICEP	28554	4308	13325	3807	3318	13350
58. ATGVSDTICEPCP	22484	4176	13463	3868	3241	13399
59. GVSdTICEPCPVG	21417	4277	13329	3584	3259	13475
60. SDTICEPCPVGFF	20192	4360	13337	3725	3358	14425
61. TICEPCPVGFFSN	25475	4390	14453	4101	3446	15502
62. CEPCPVGFFSNVS	26387	4419	14370	4434	3538	14441
63. PCPVGFFSNVSSA	40241	4468	14425	4363	3409	14664
64. PVGFFSNVSSAFE	27432	11225	85432	4772	5735	49493
65. GFFSNVSSAFEKC	77408	4483	14462	4173	3489	14521
66. FSNVSSAFEKCHP	57923	4088	14050	4230	3296	13989
67. NVSSAFEKCHPWT	23154	4031	13752	4025	3343	13619
68. SSAFEKCHPWTSC	20994	4170	13512	4006	3419	13466
69. AFEKCHPWTSCET	21390	4498	13629	4028	3413	13518
70. EKCHPWTSCETKD	19639	4186	13571	3911	3403	16038
71. CHPWTSCETKDLV	20967	4216	13608	4177	3489	13283
72. PWTSCETKDLVVQ	23271	4300	13420	4459	3316	13507
73. TSCETKDLVVQQA	26353	4690	13457	4411	3496	13462
74. CETKDLVVQQAGT	26955	4517	13389	4600	3403	13433
75. TKDLVVQQAGTNK	63164	6695	13475	60382	7609	13271
76. DLVVQQAGTNKTD	25820	4567	13537	4057	3585	13328
77. VVQQAGTNKTDVV	28426	4587	13372	4179	3418	13309
78. QQAGTNKTDVVCQ	19474	4111	13455	3709	3809	13332
79. AGTNKTDVVCQPQ	18988	4186	13517	3868	3231	13436
80. TNKTDVVCQPQDR	18178	4662	13423	3654	4897	13350
81. KTDVVCQPQDRLR	27431	4208	13879	4242	4238	13779
82. DVVCQPQDRLRAL	28872	4127	14128	4179	3459	13855

Fig. 2A

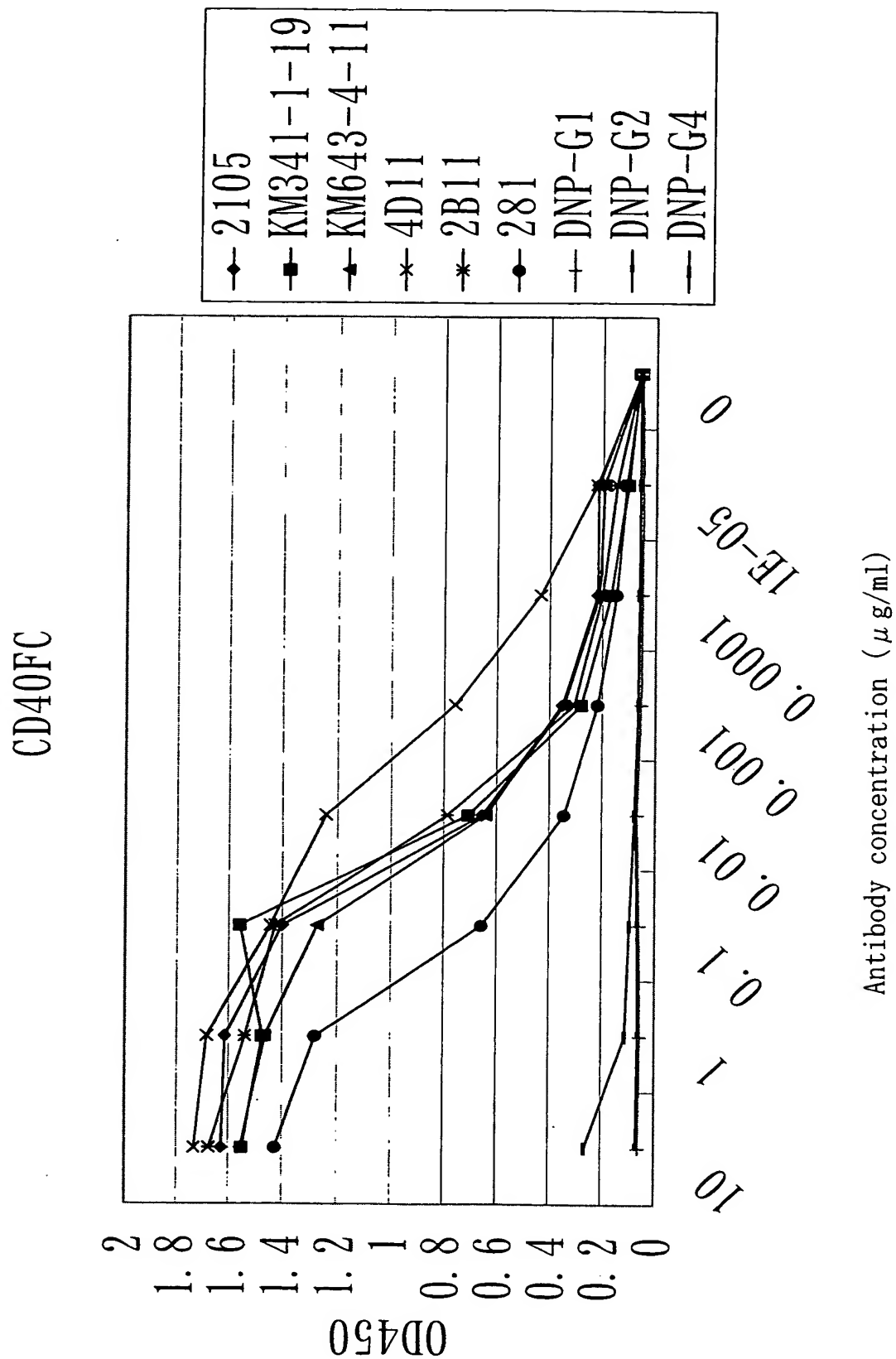


Fig. 2B

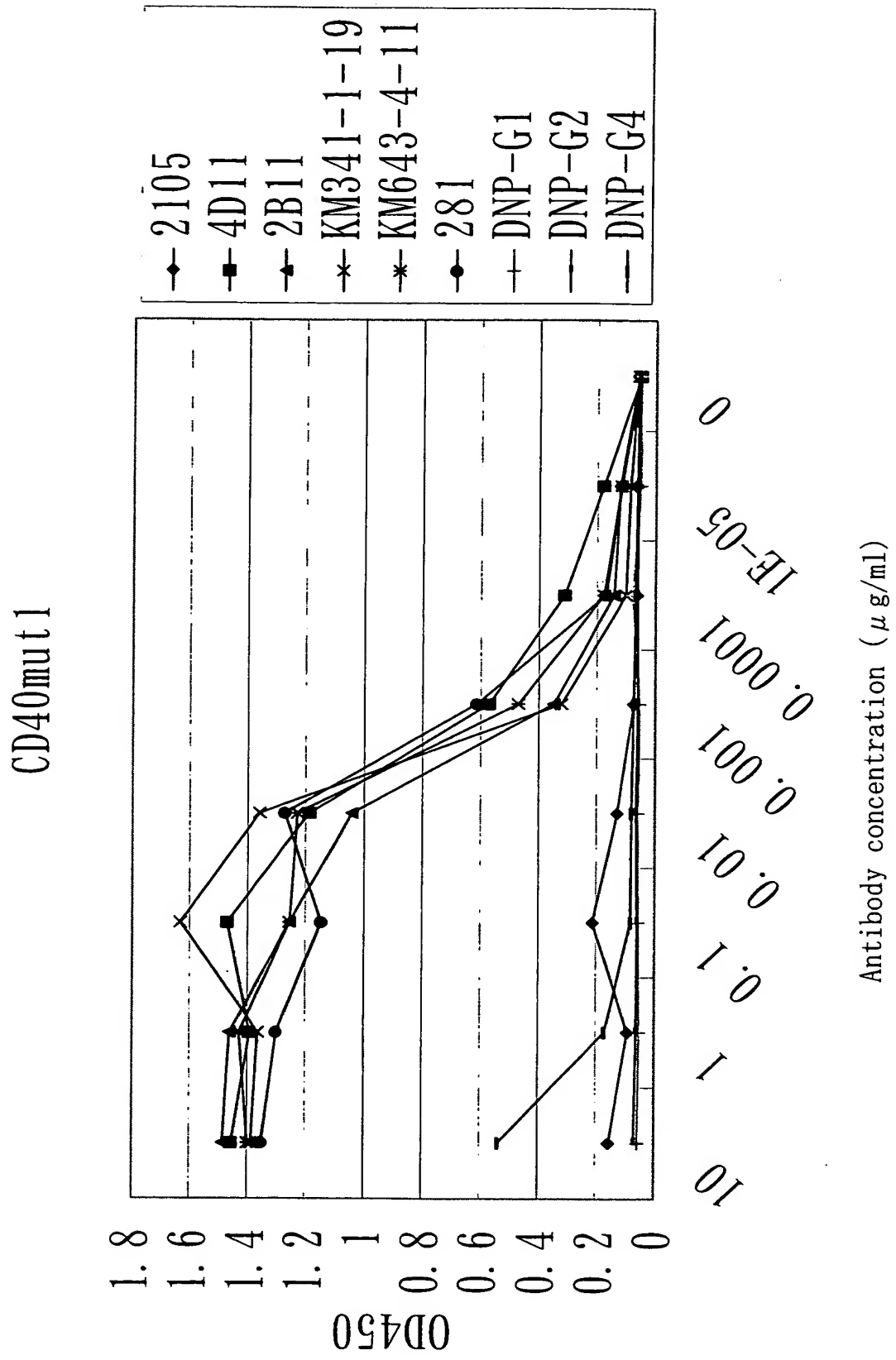


Fig. 2C

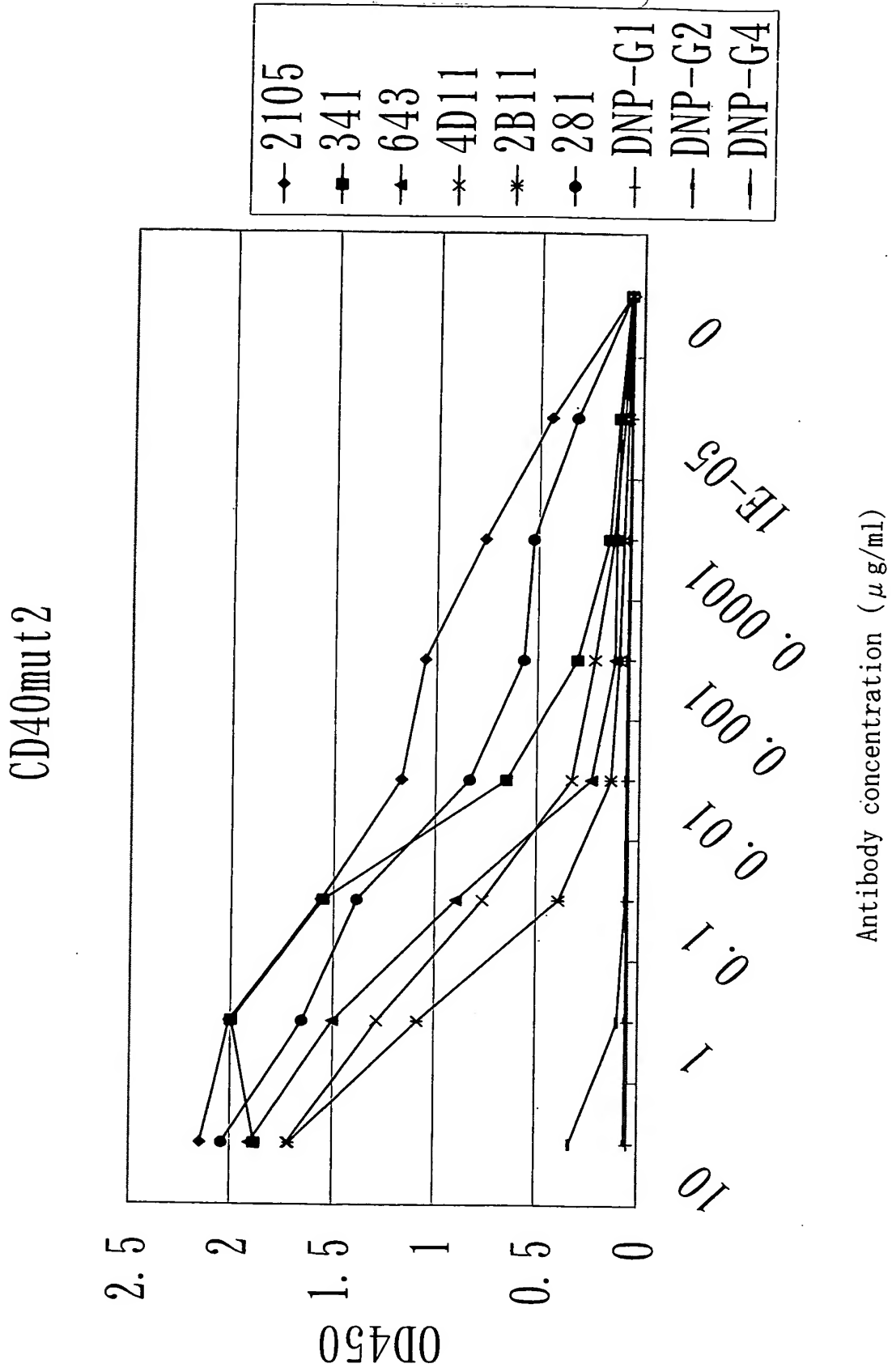
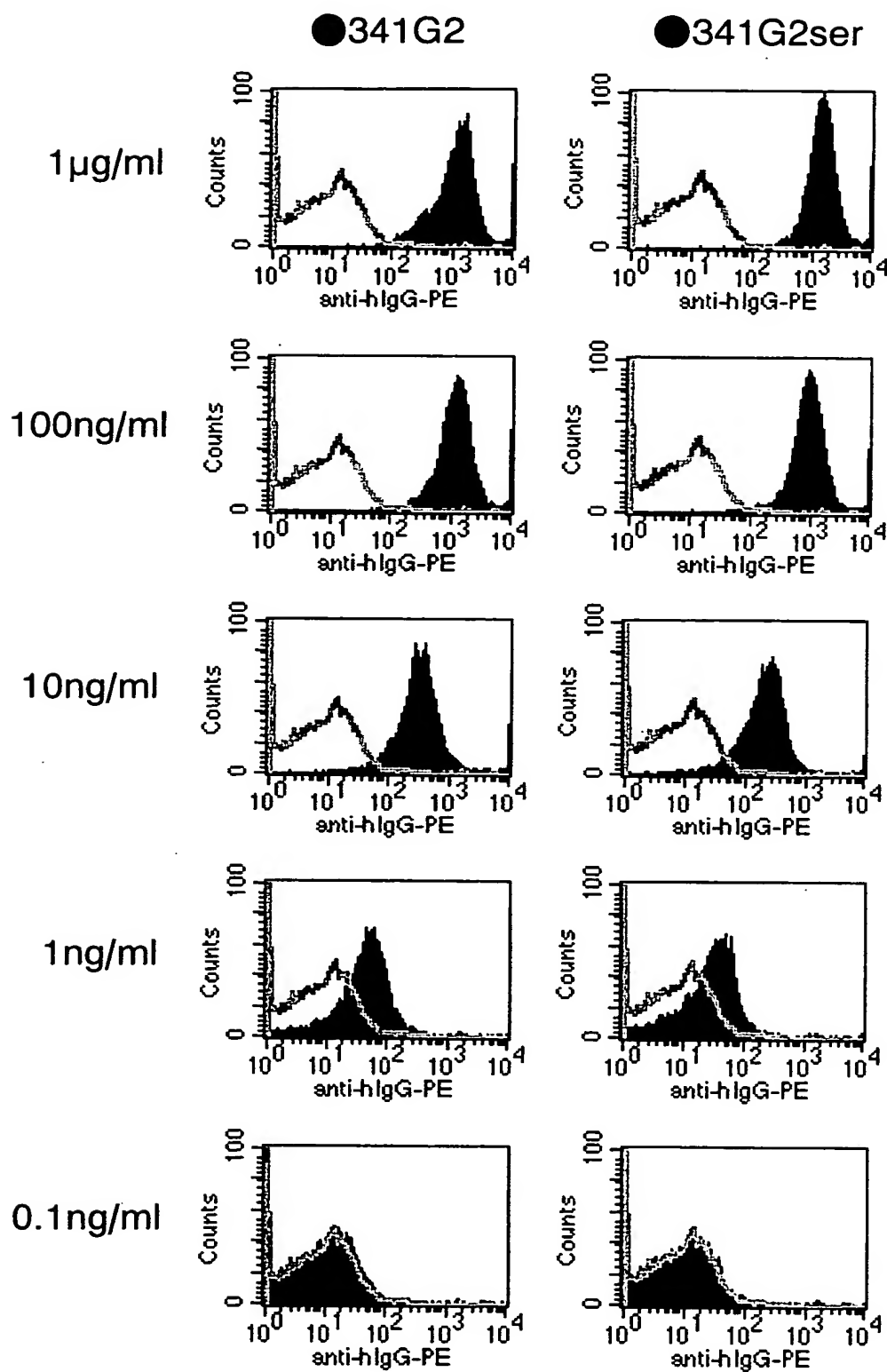


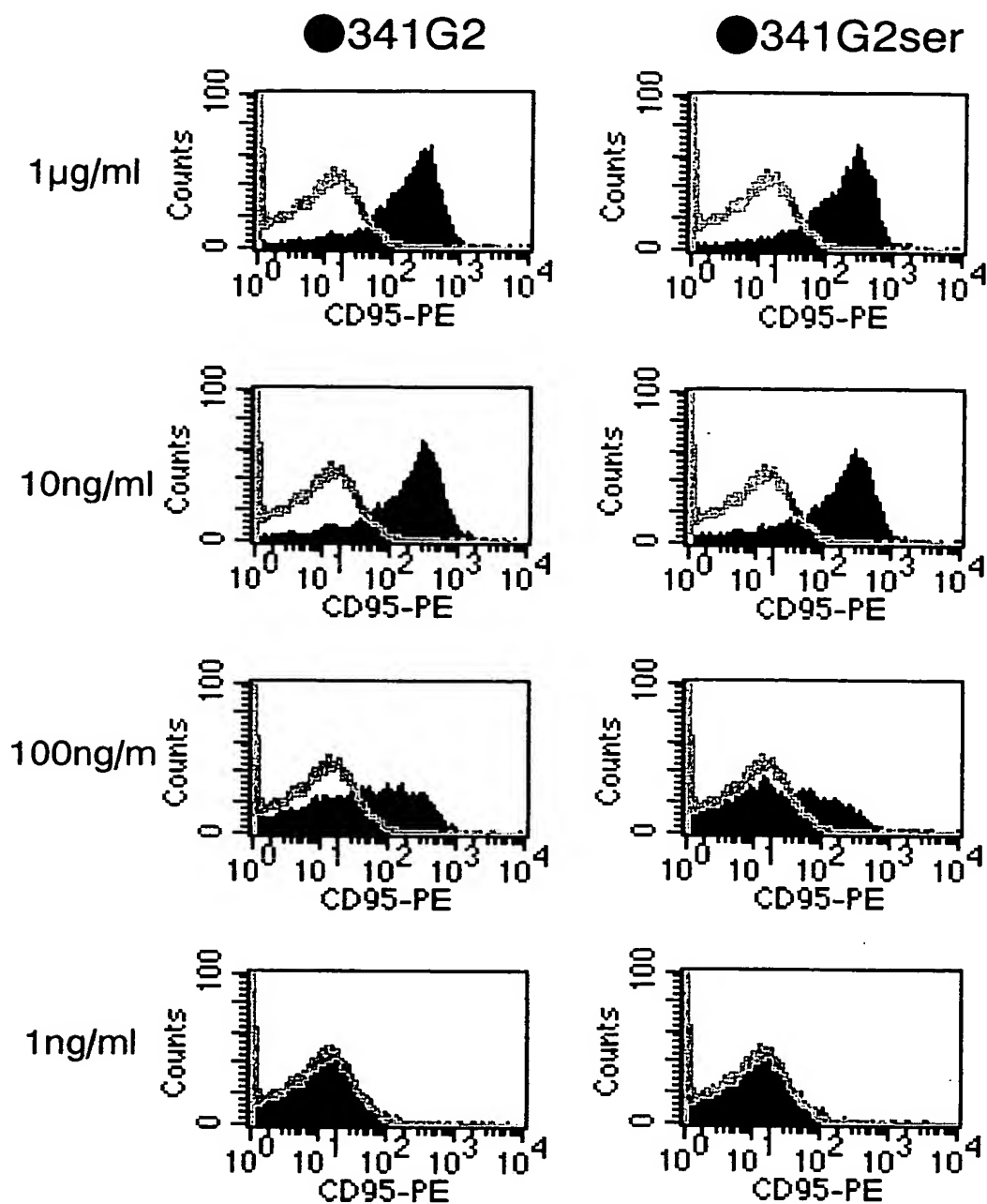
Fig. 3A



BEST AVAILABLE COPY



Fig. 3B



BEST AVAILABLE COPY

**Fig. 4A**

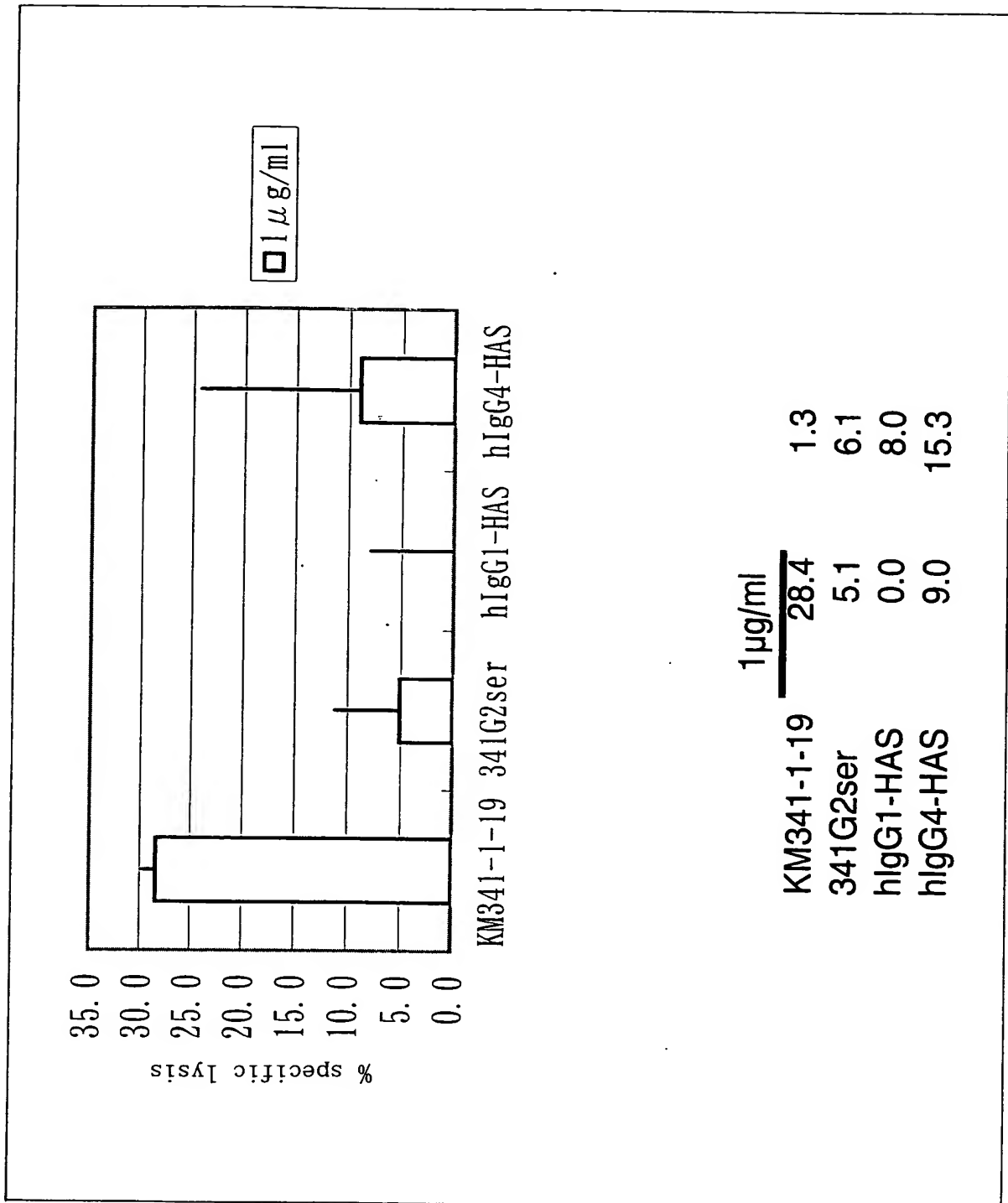


Fig. 4B

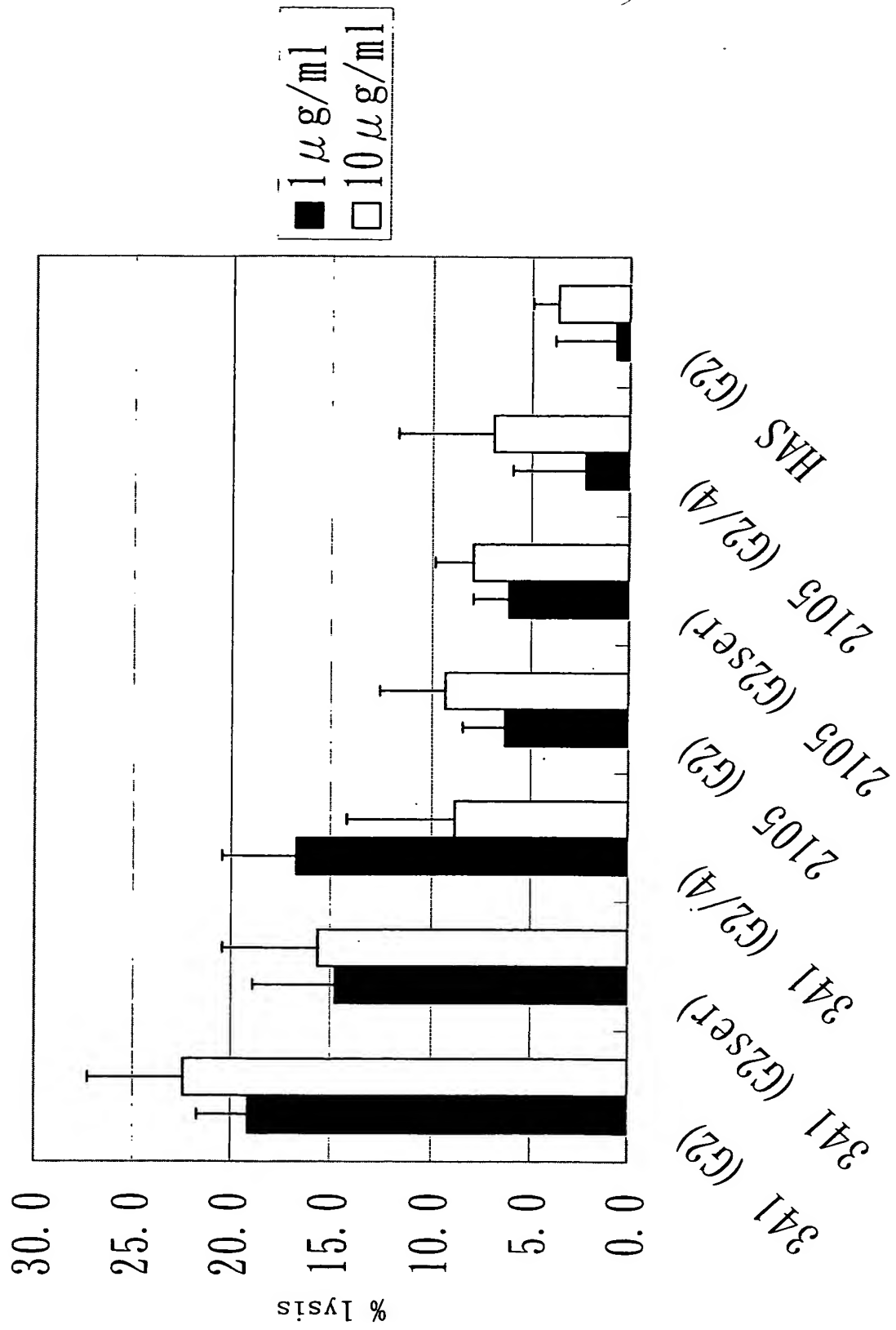


Fig. 5A-1 [2105]

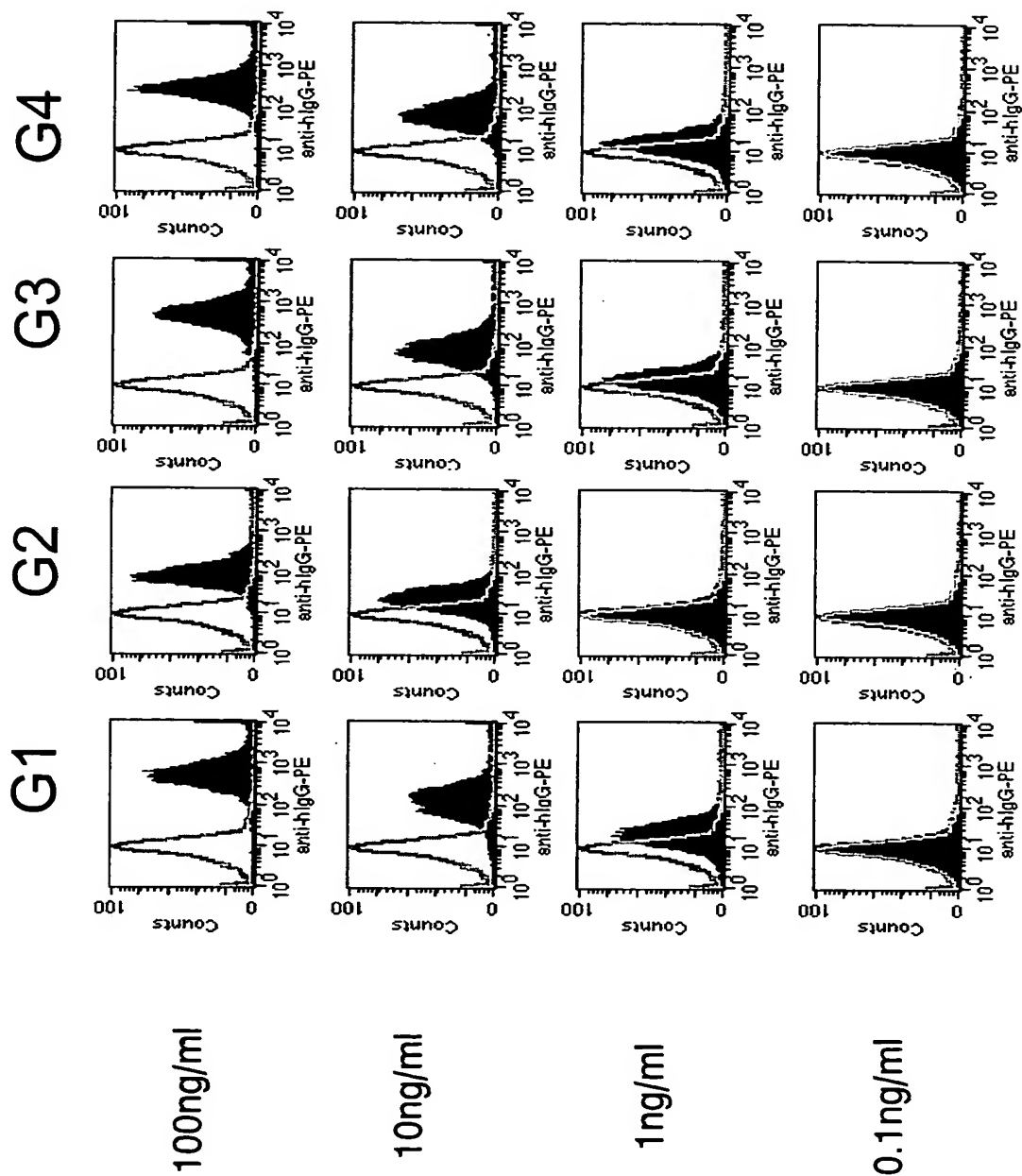


Fig. 5A-2

[ 341 ]

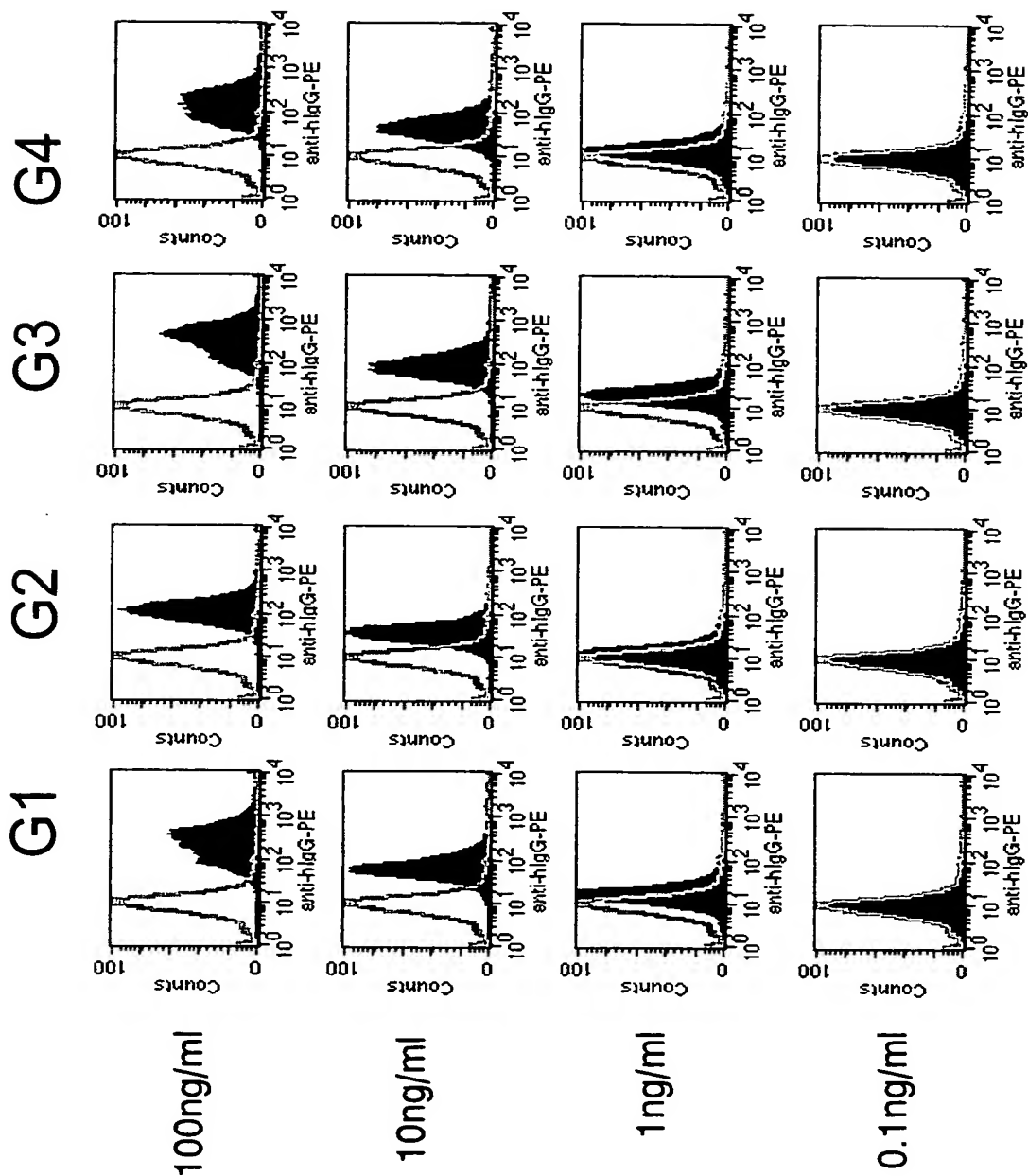


Fig. 5B-1

[2105]

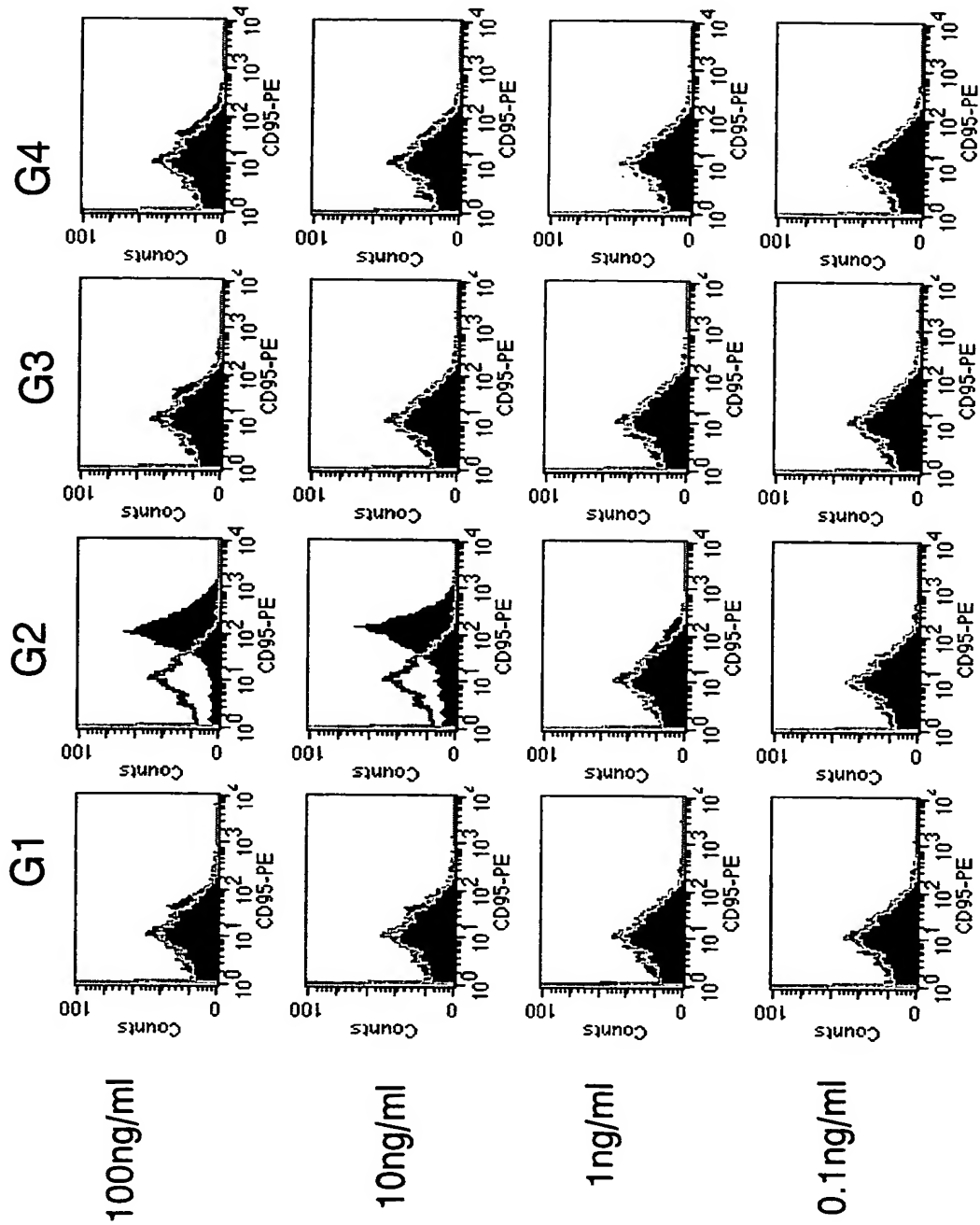


Fig. 5B-2

[341]

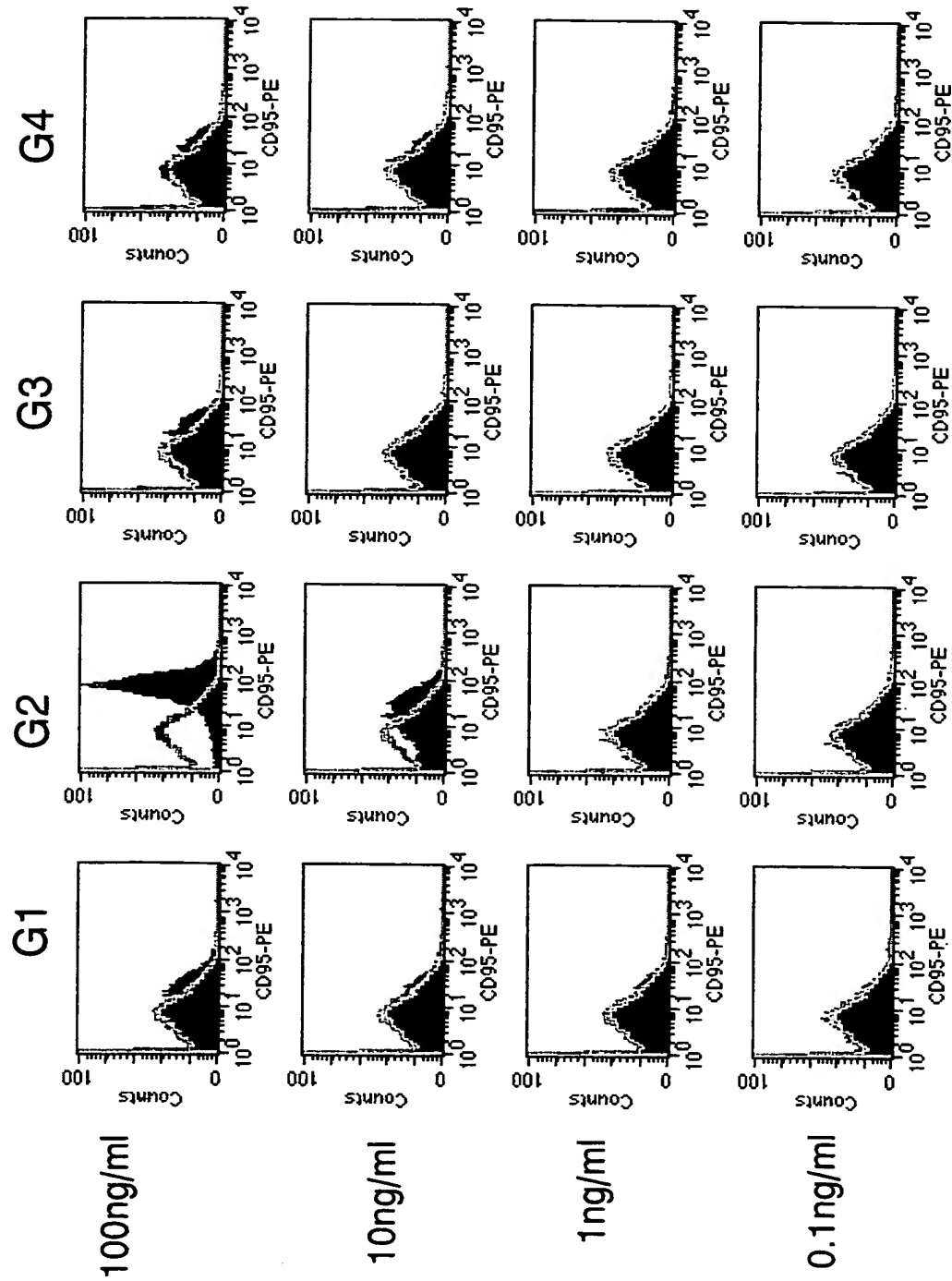


Fig. 6A-1

[341]

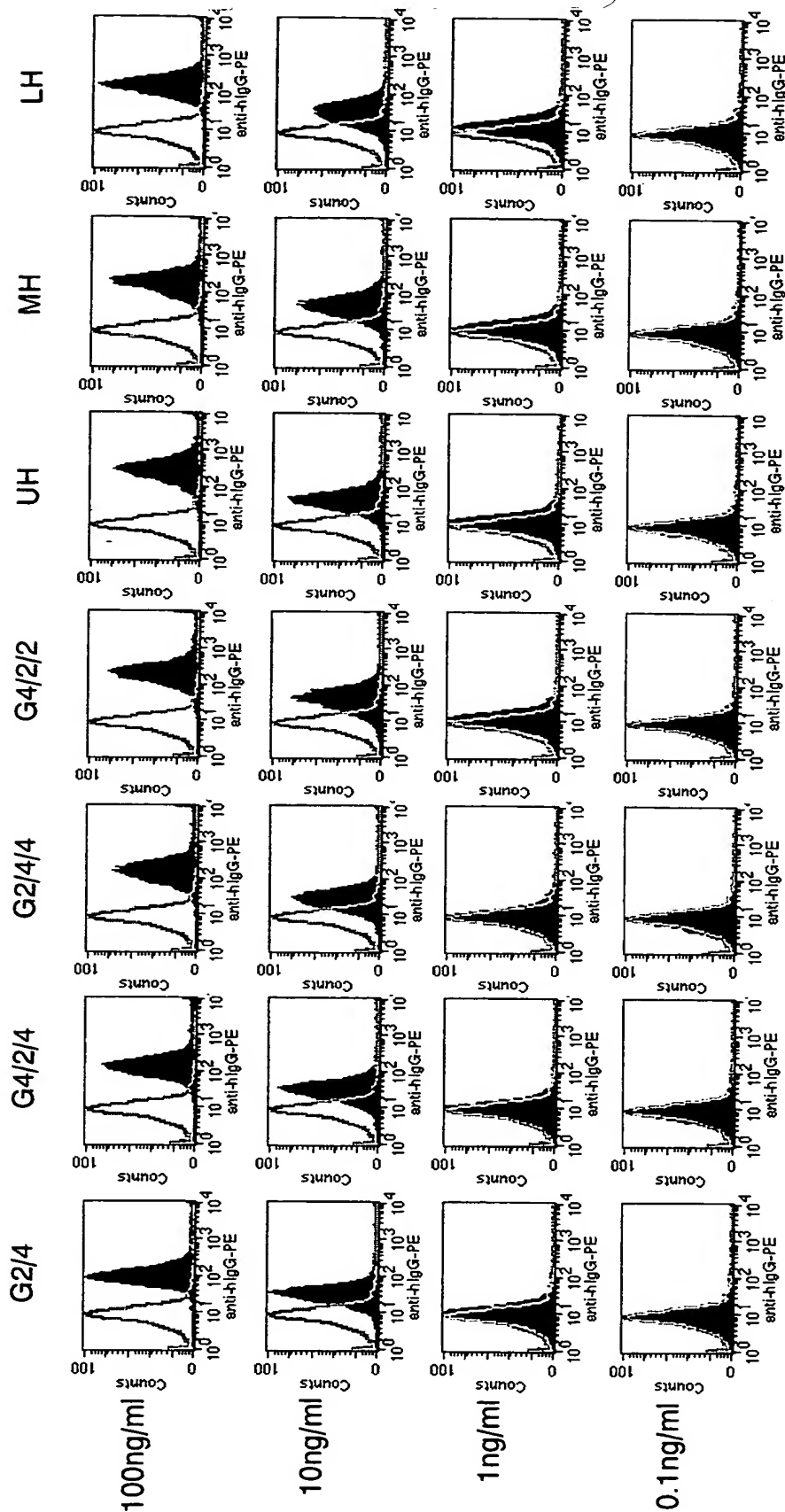




Fig. 6A-2

[2105]

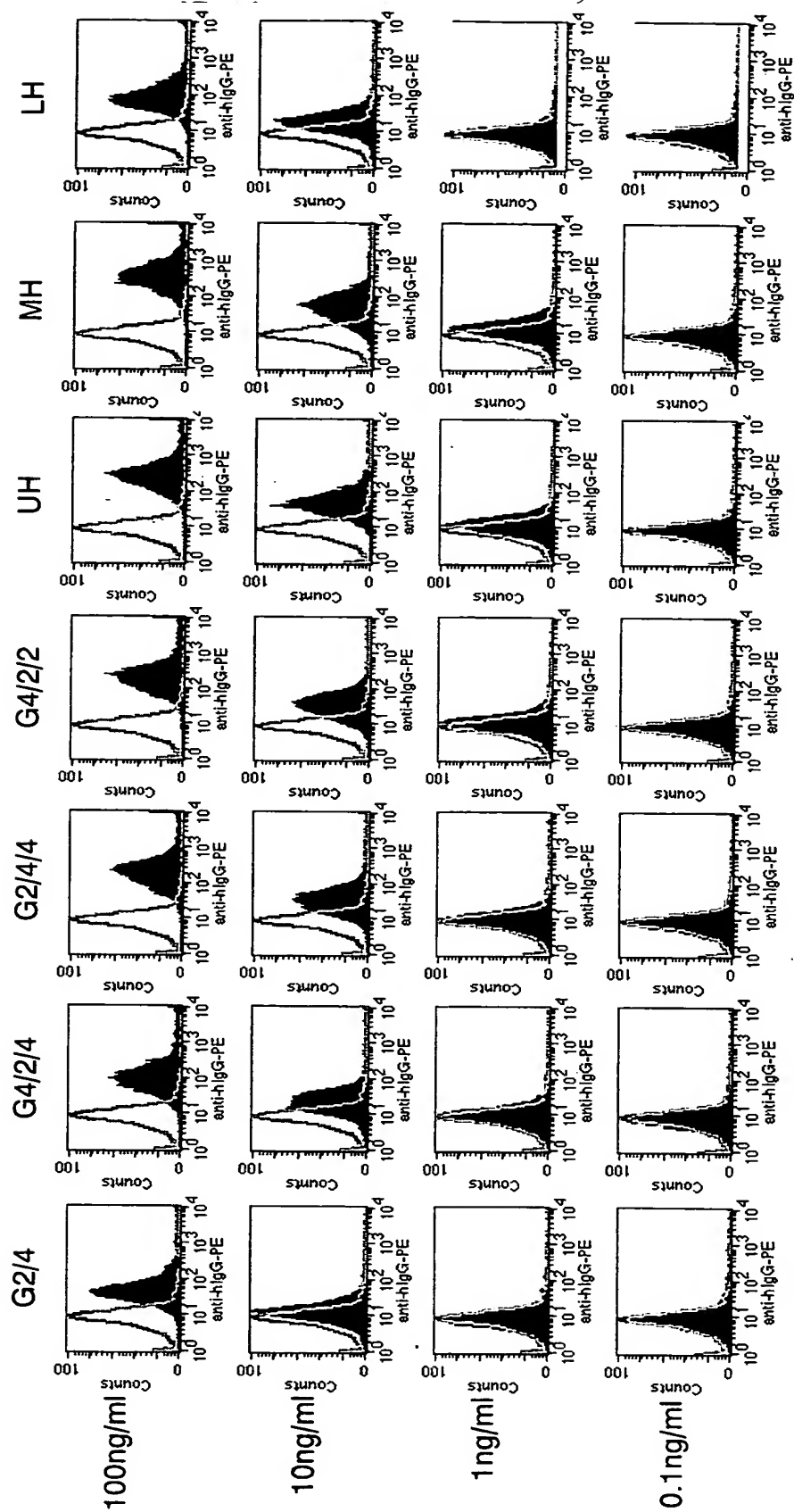


Fig. 6B-1

[341]

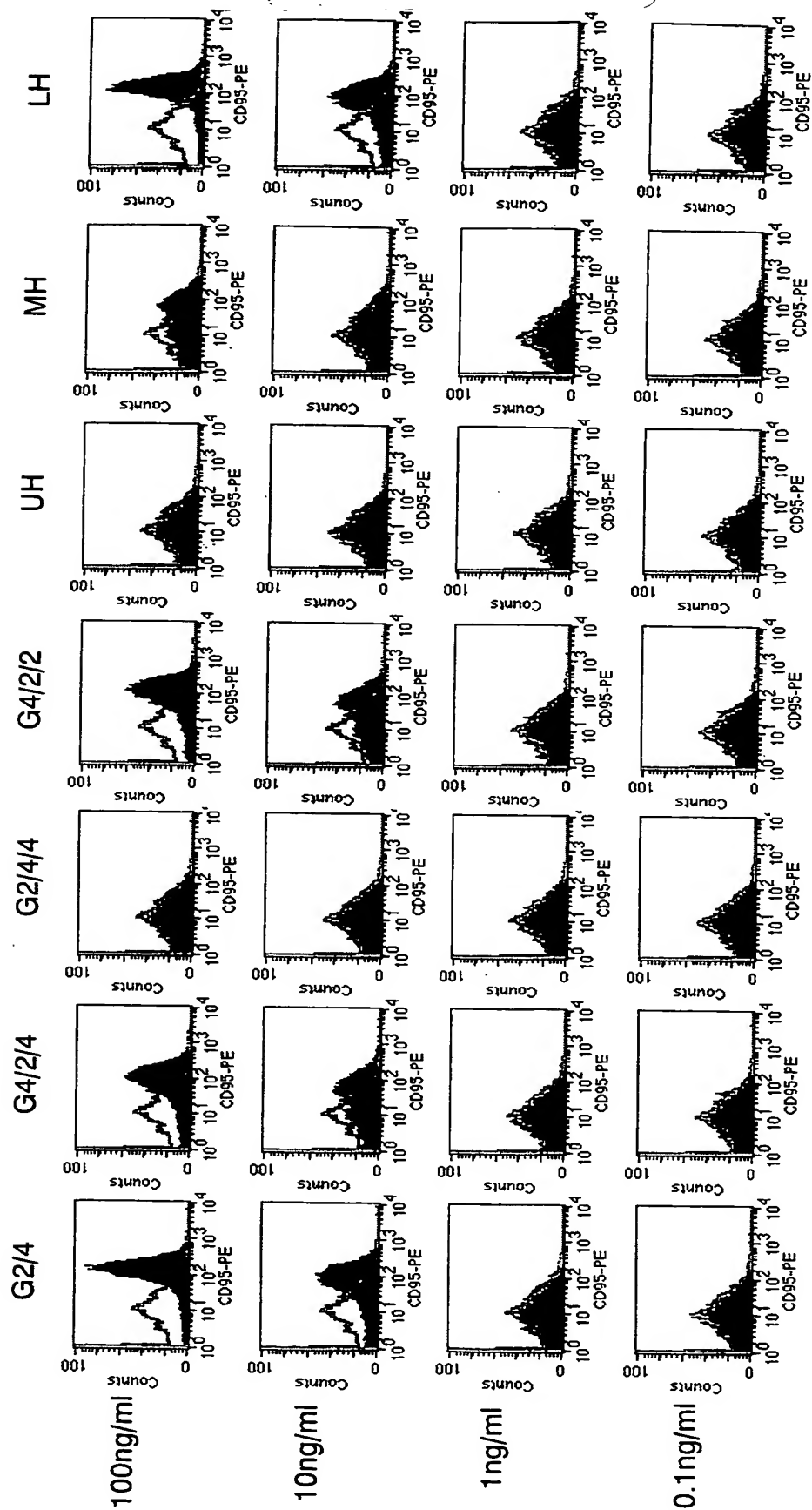


Fig. 6B-2

[2105]

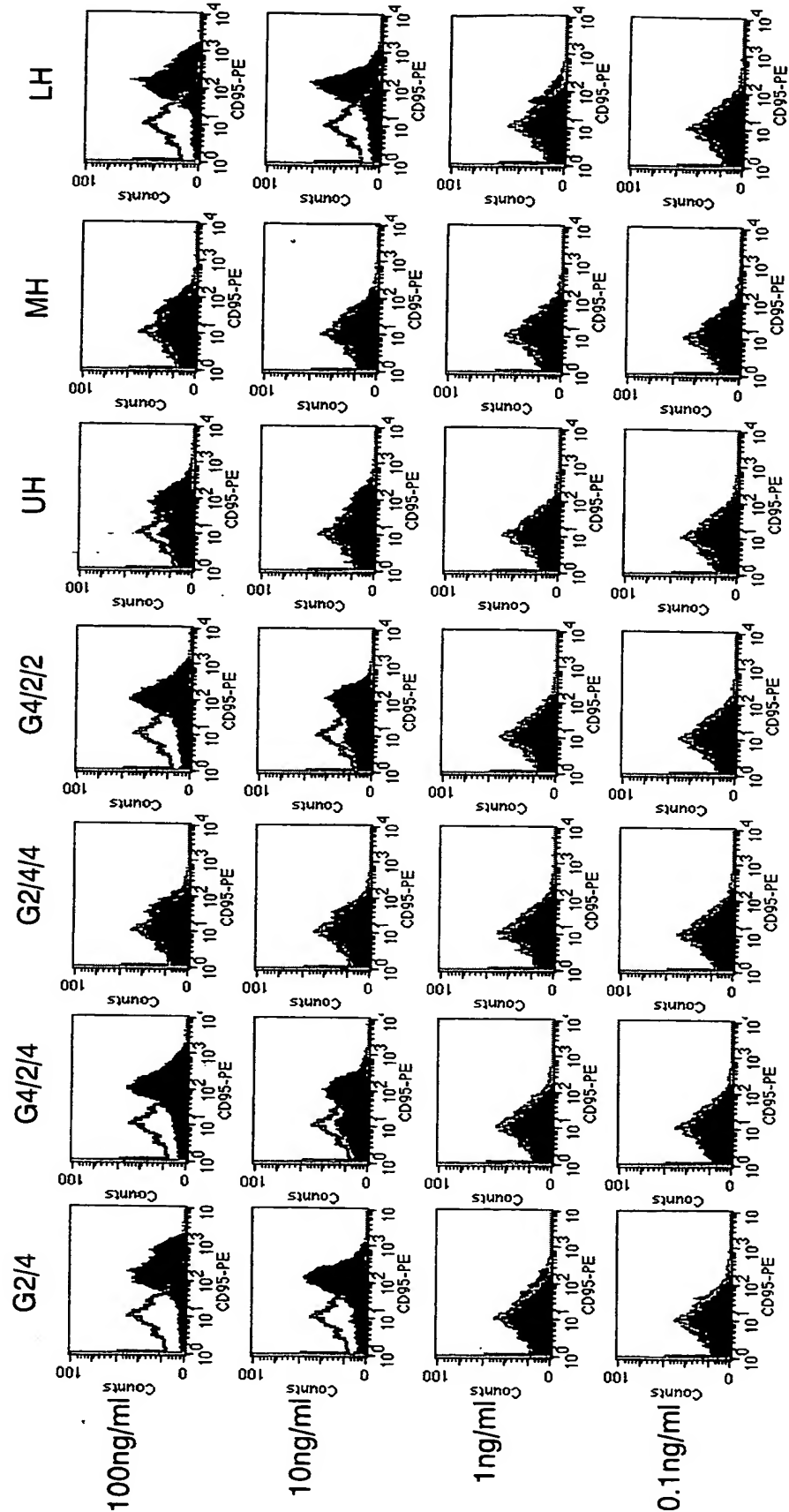


Fig. 7A

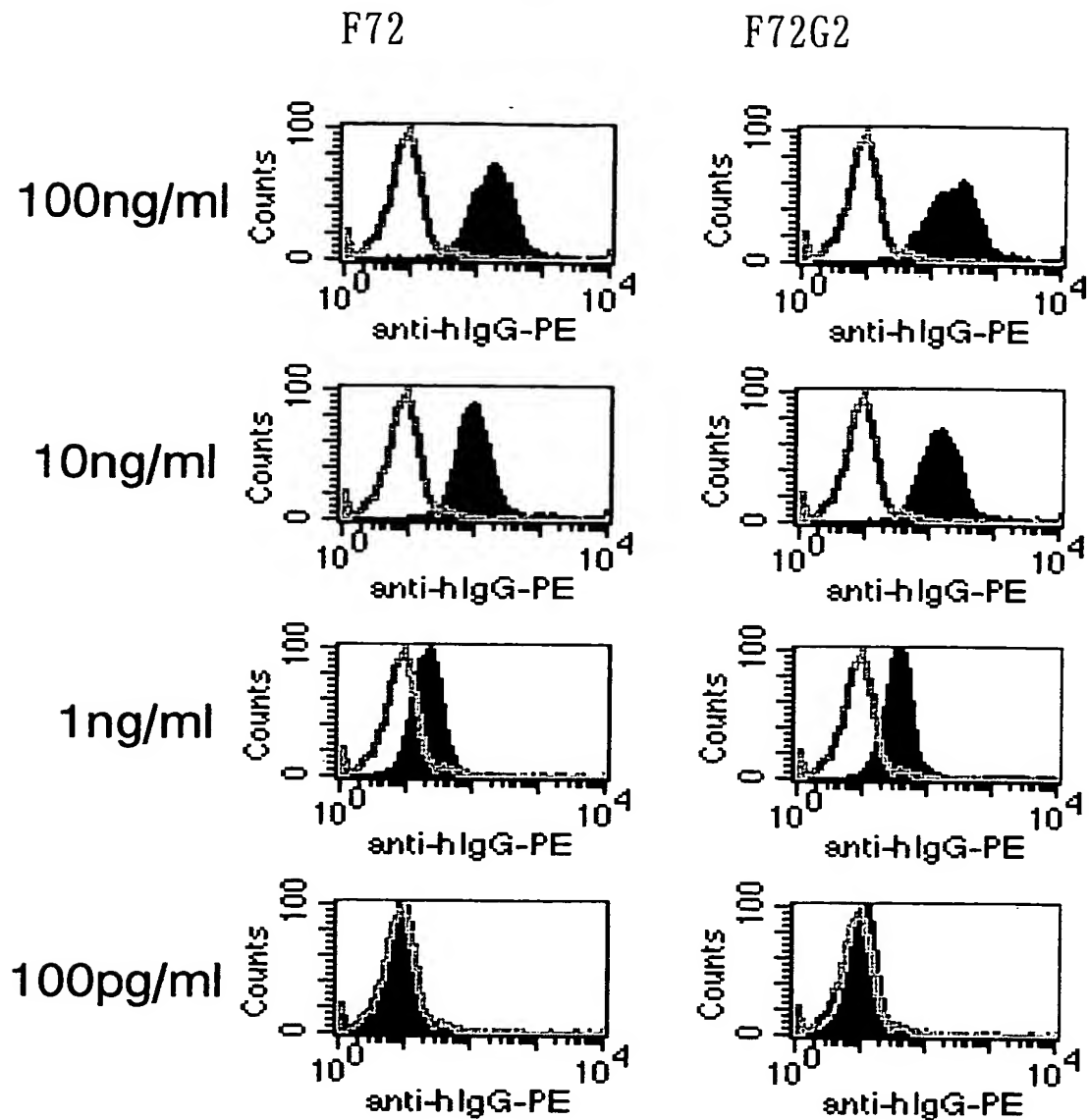


Fig. 7B

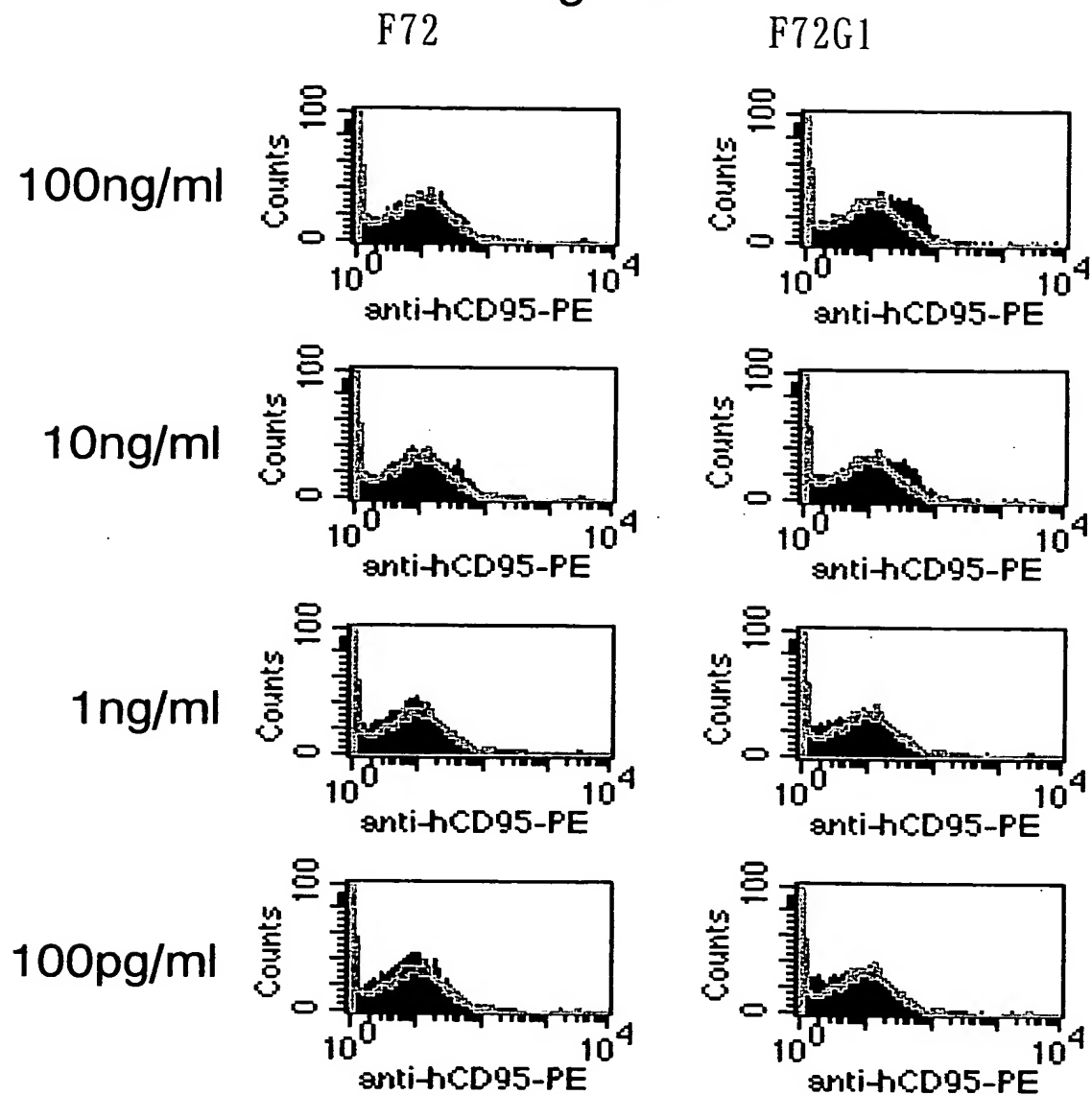


Fig. 8A

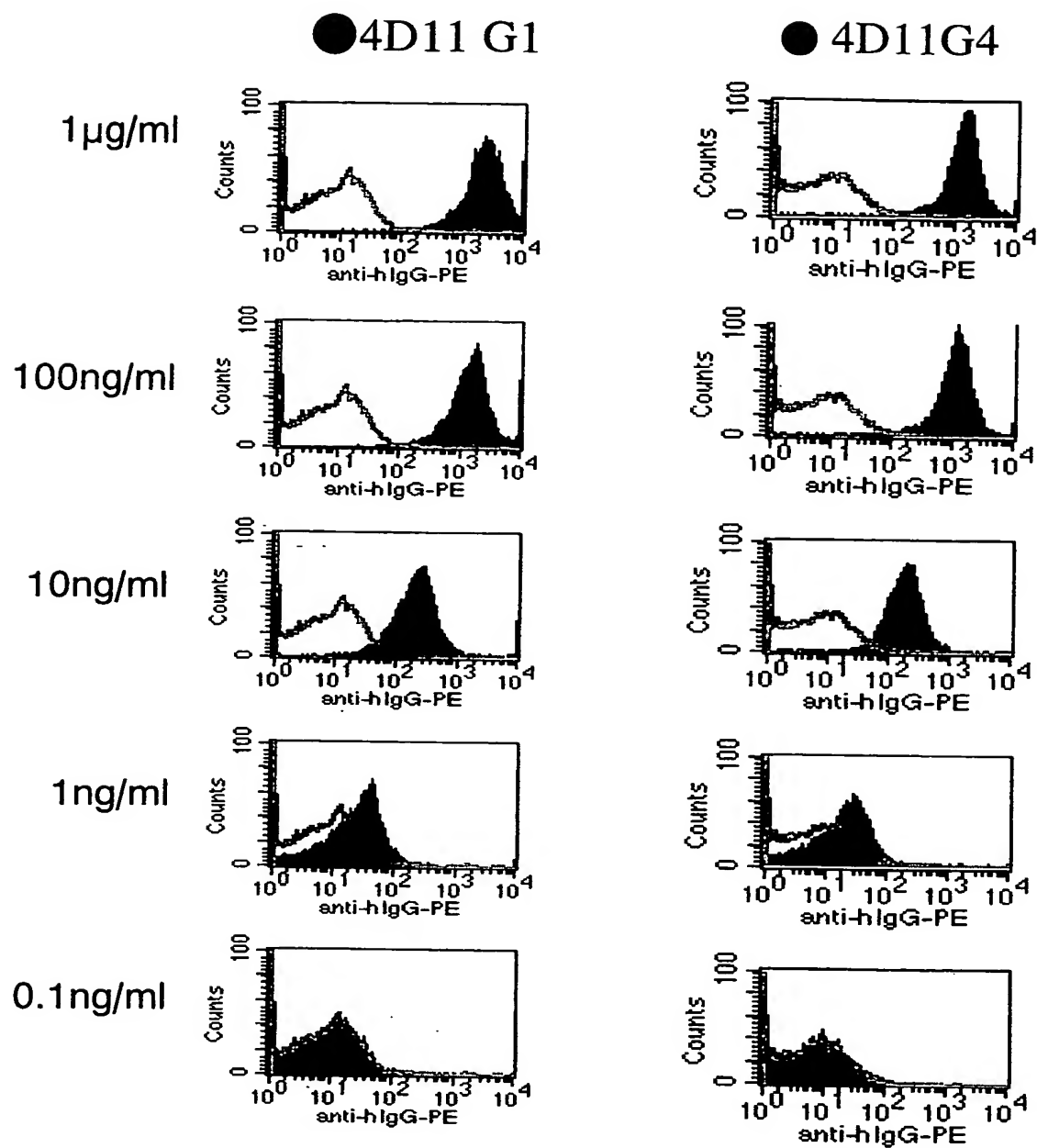


Fig. 8B

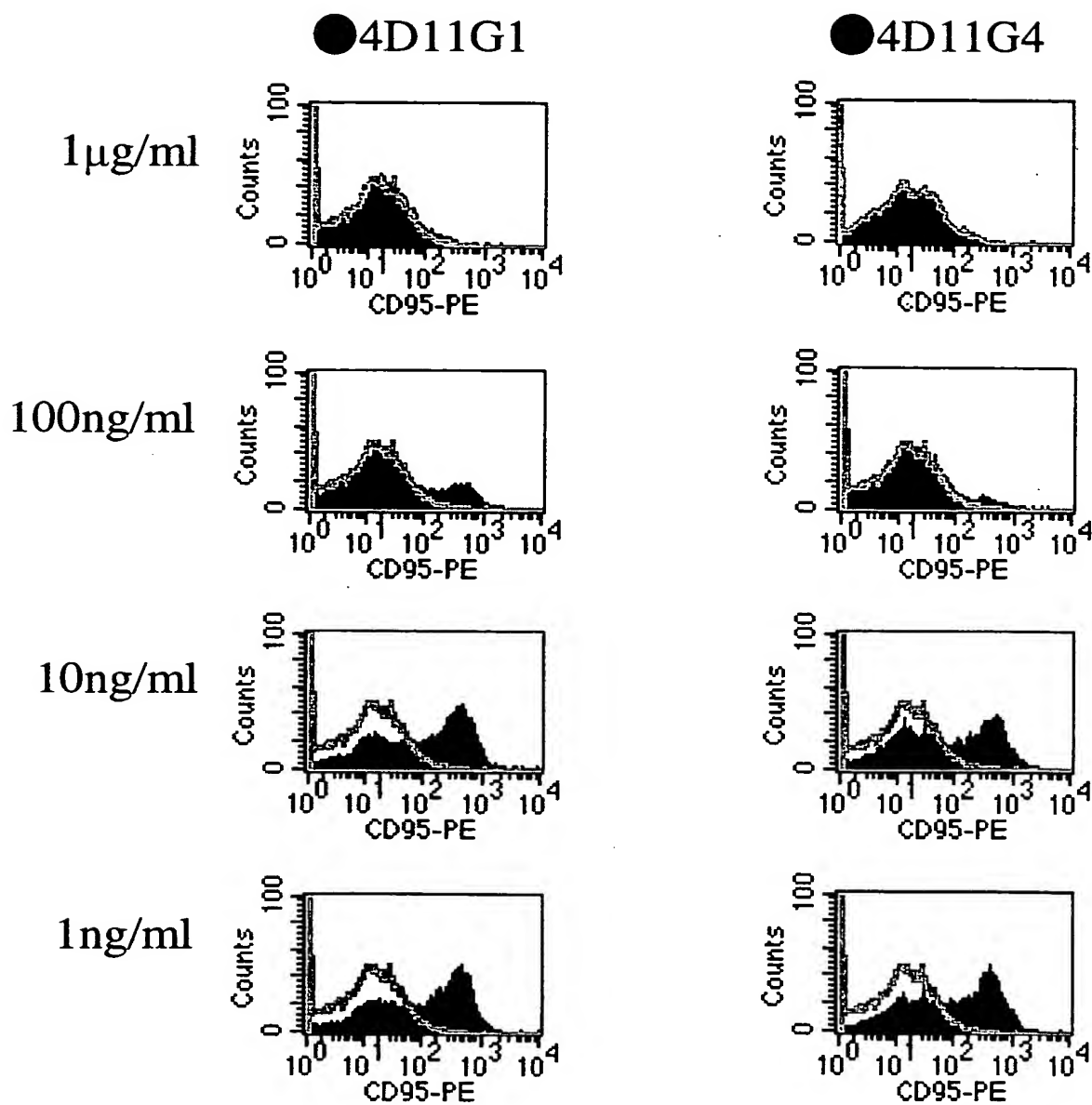


Fig. 9

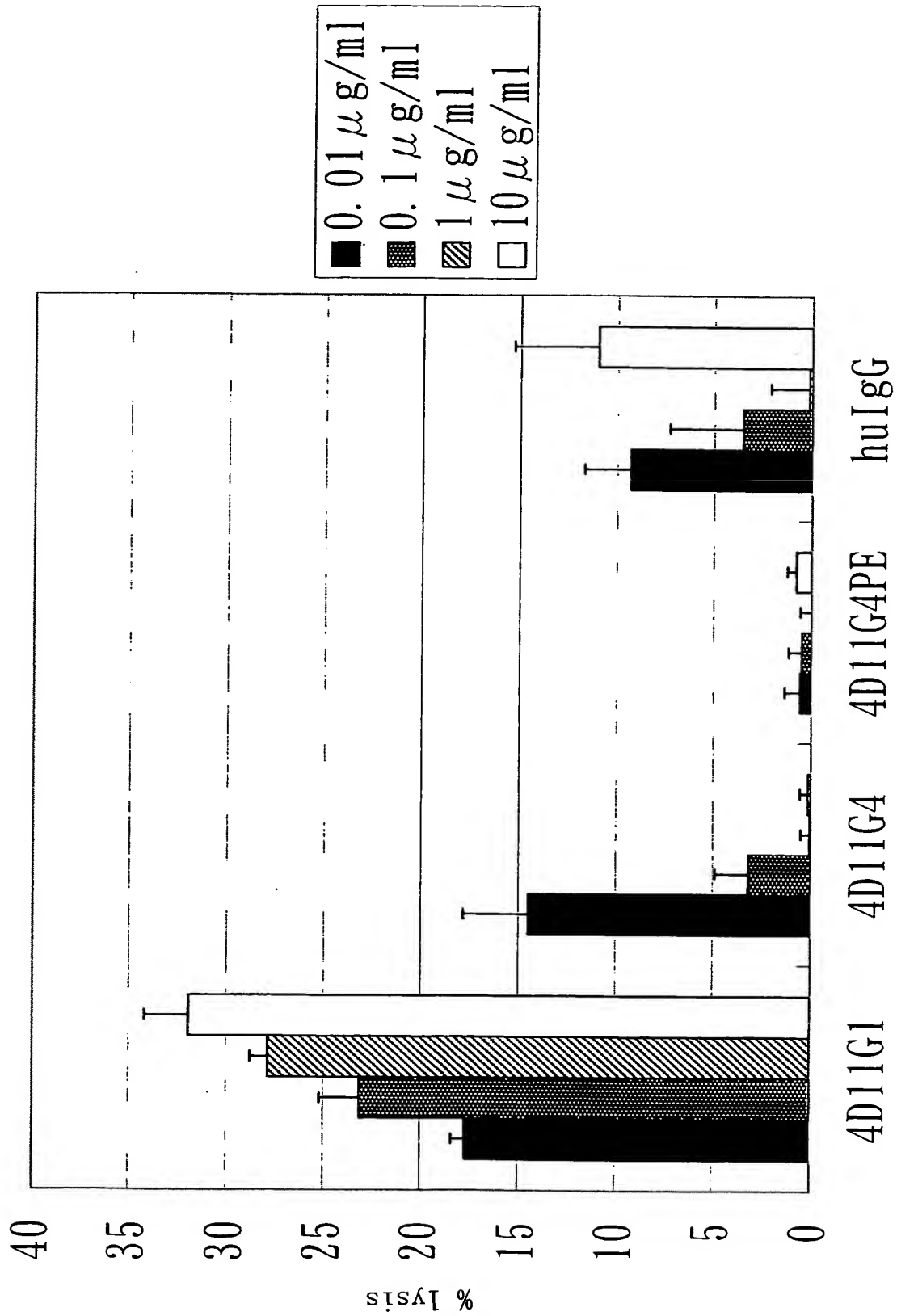
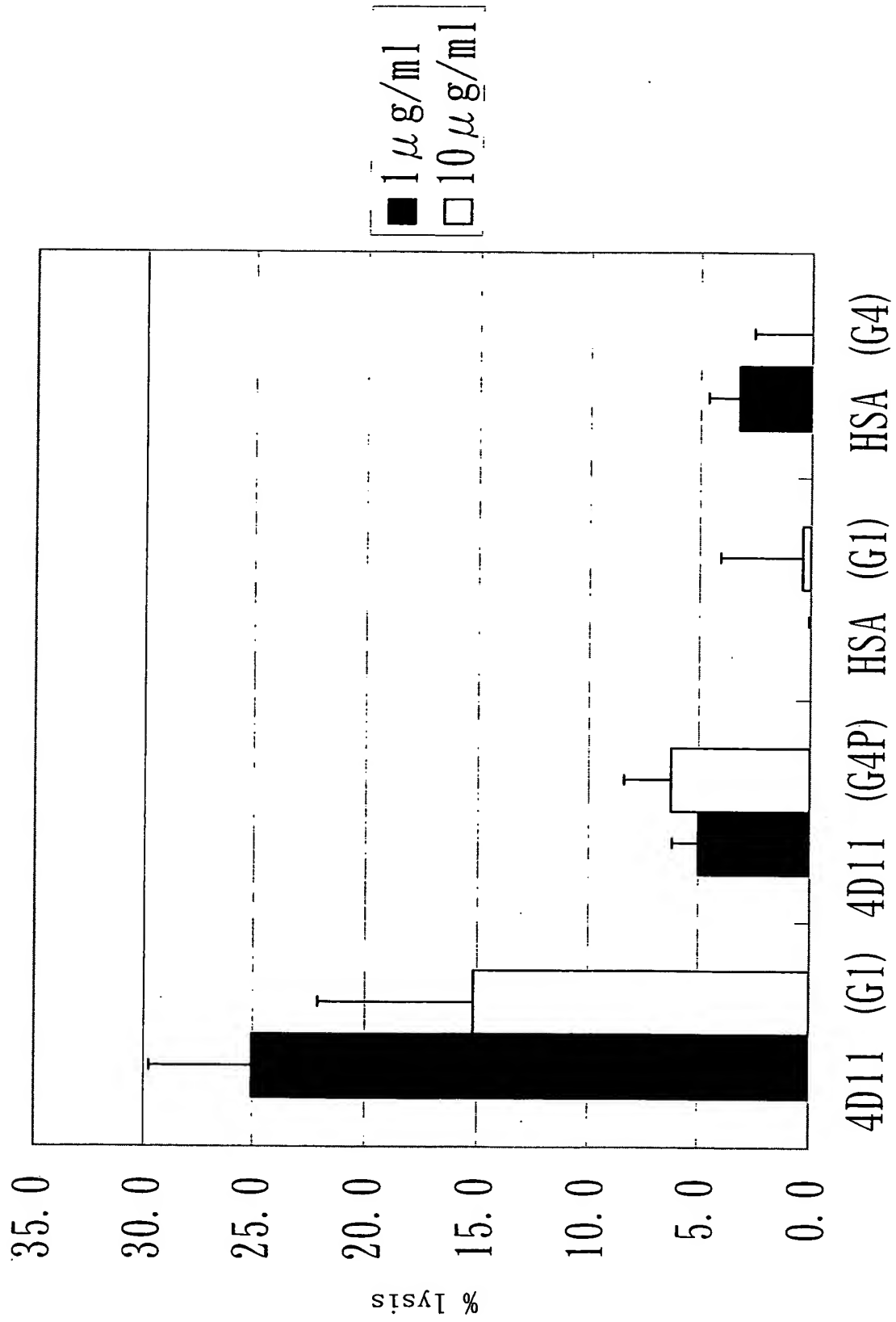




Fig. 10



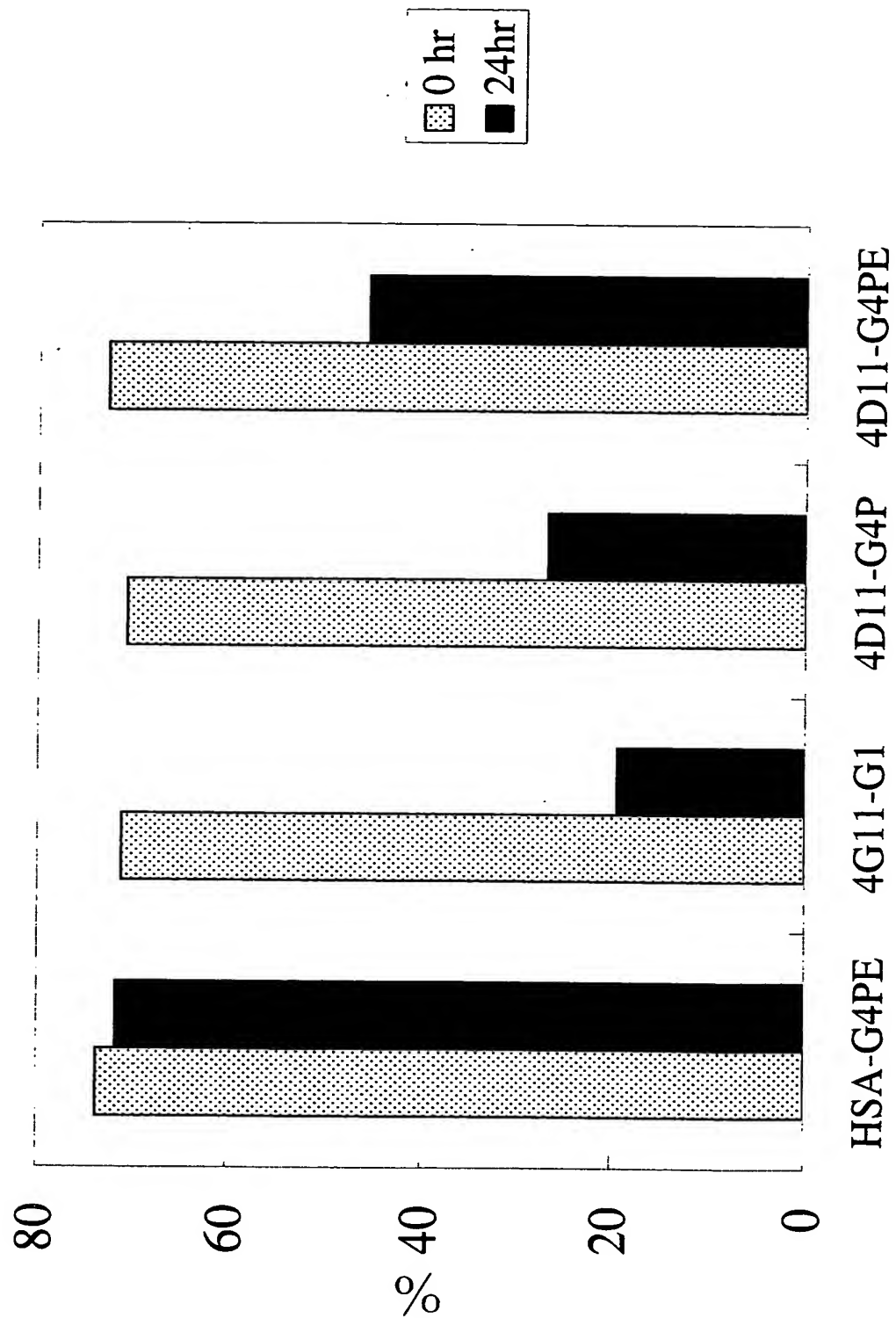


Fig. 11

Fig. 12A

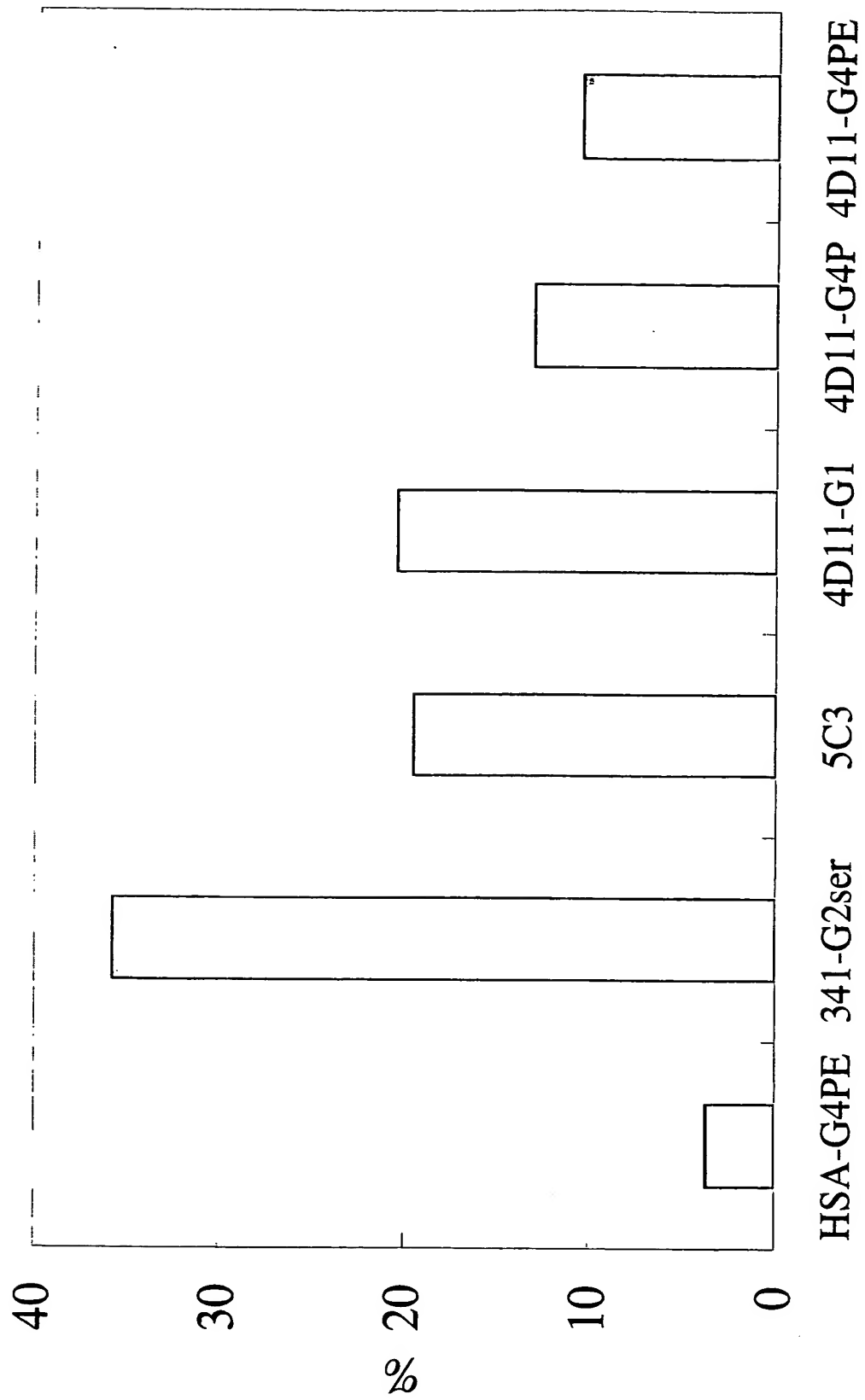


Fig. 12B

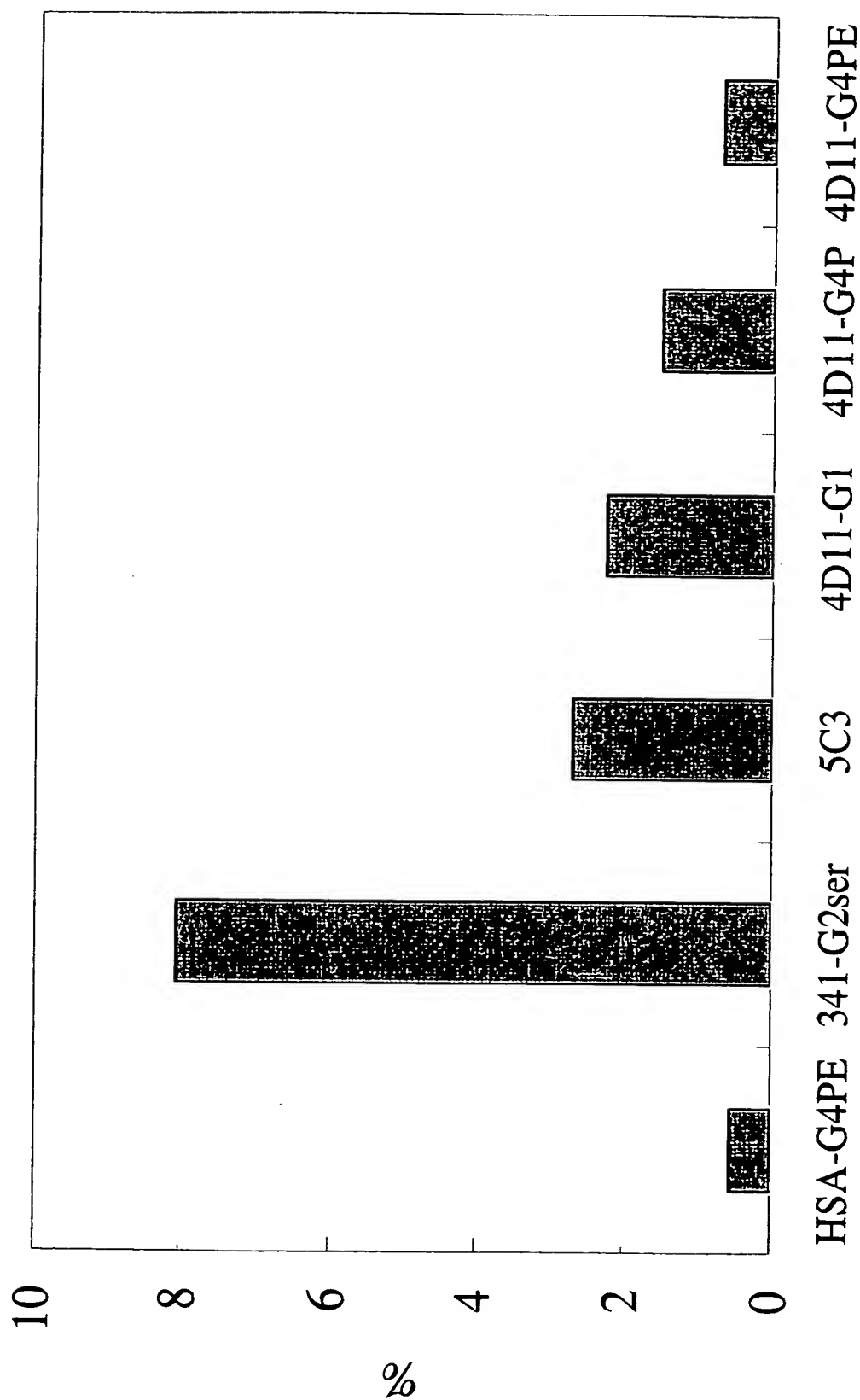


Fig. 12C

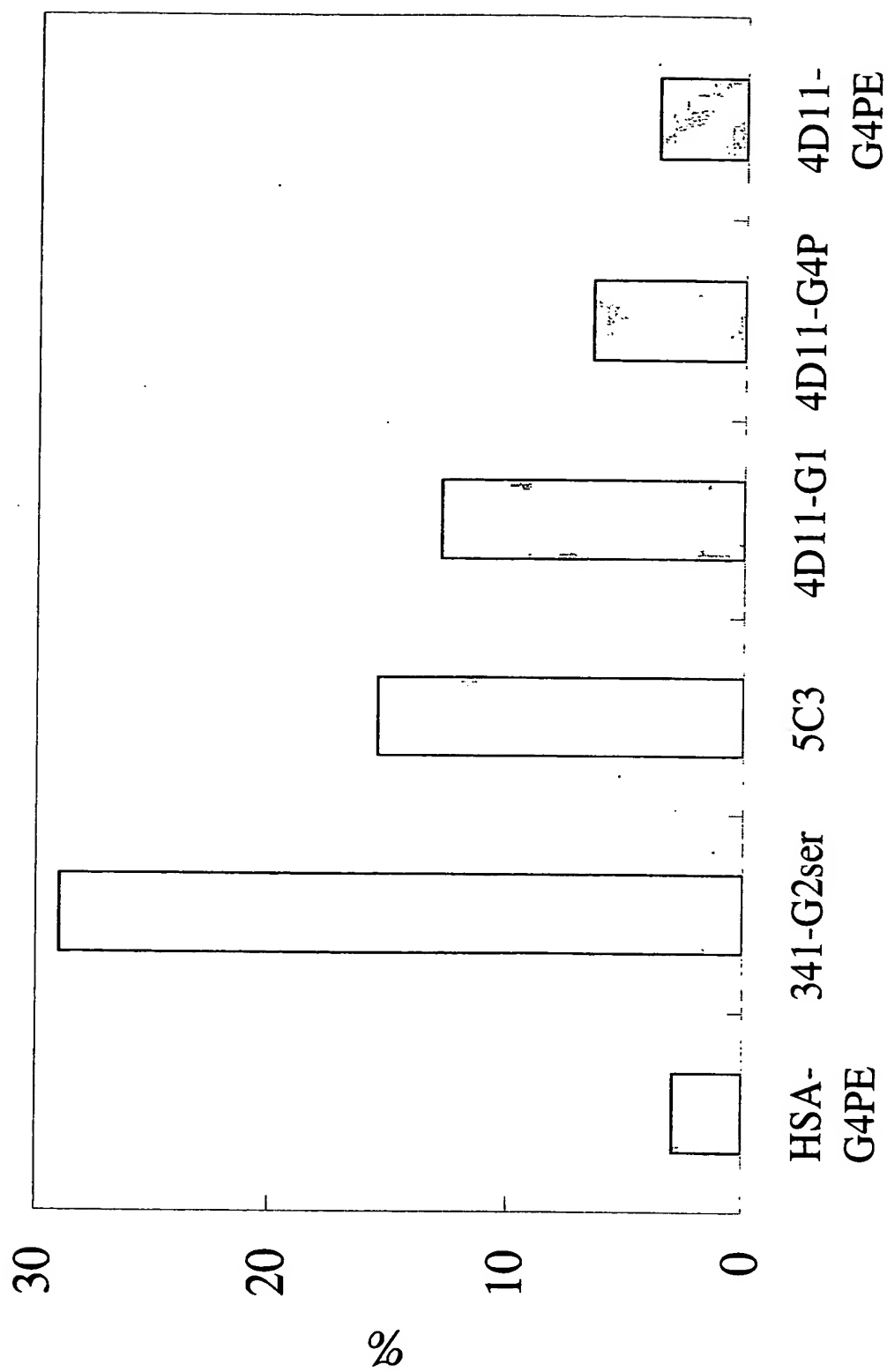


Fig. 13A

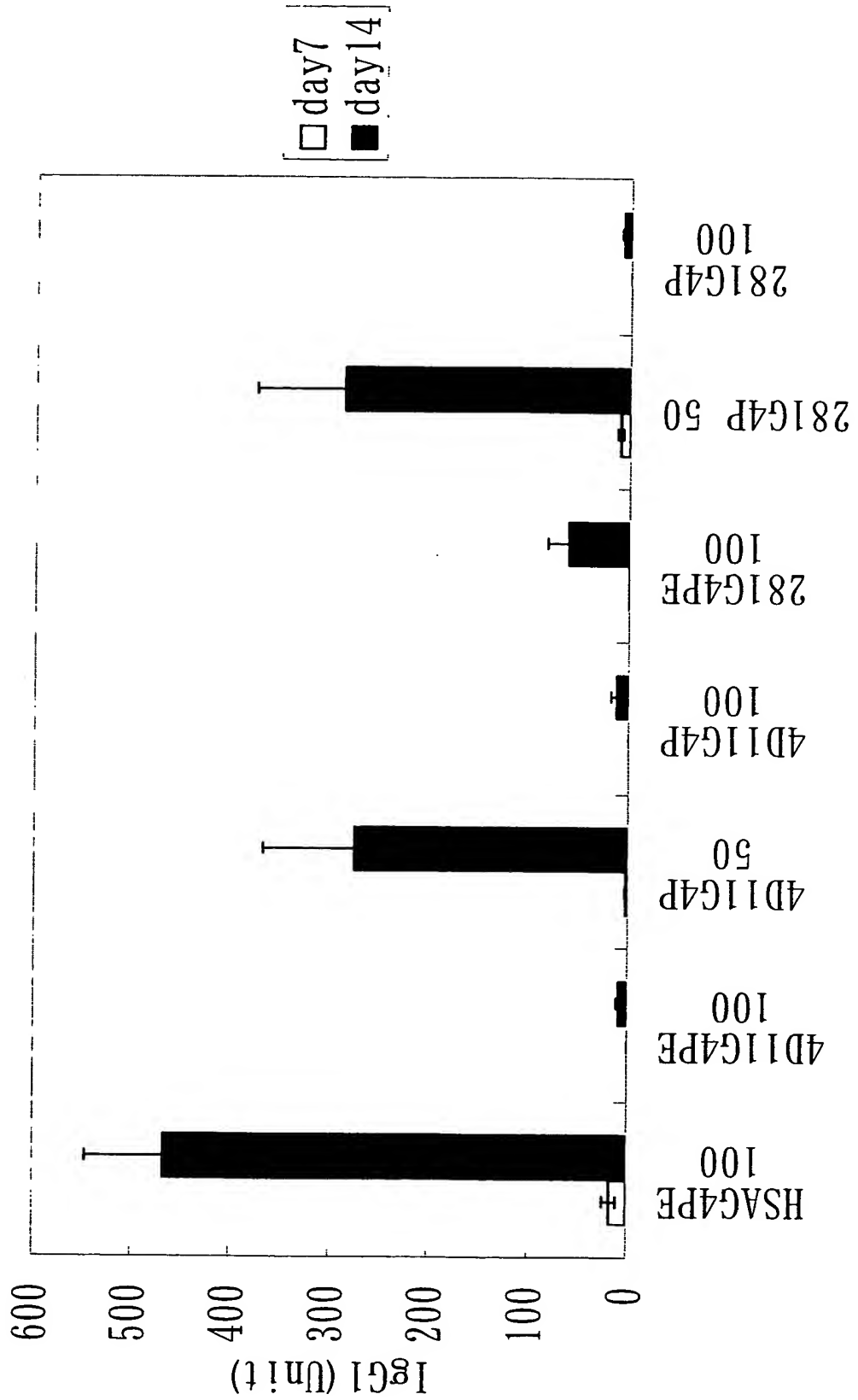


Fig. 13B

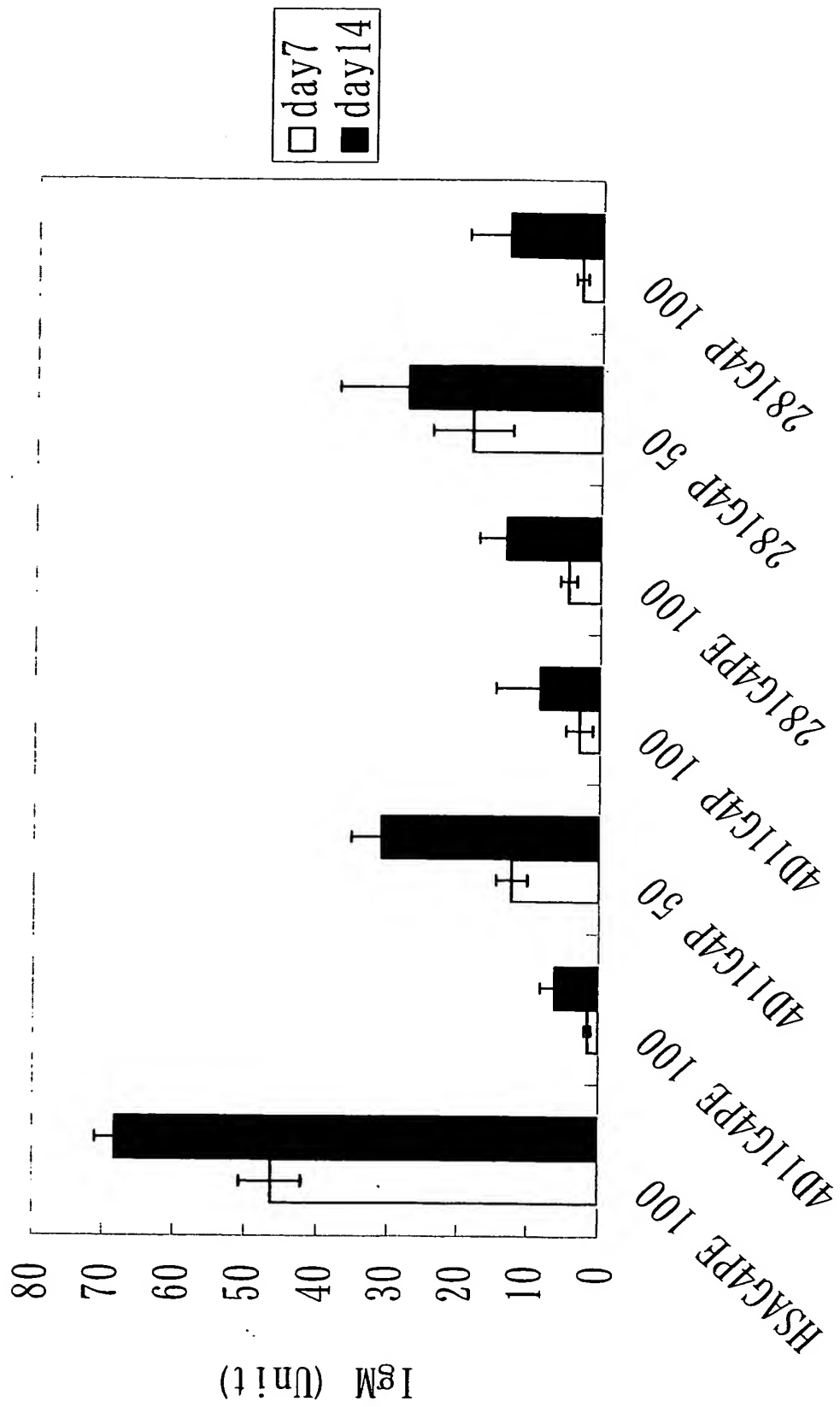


Fig. 14A

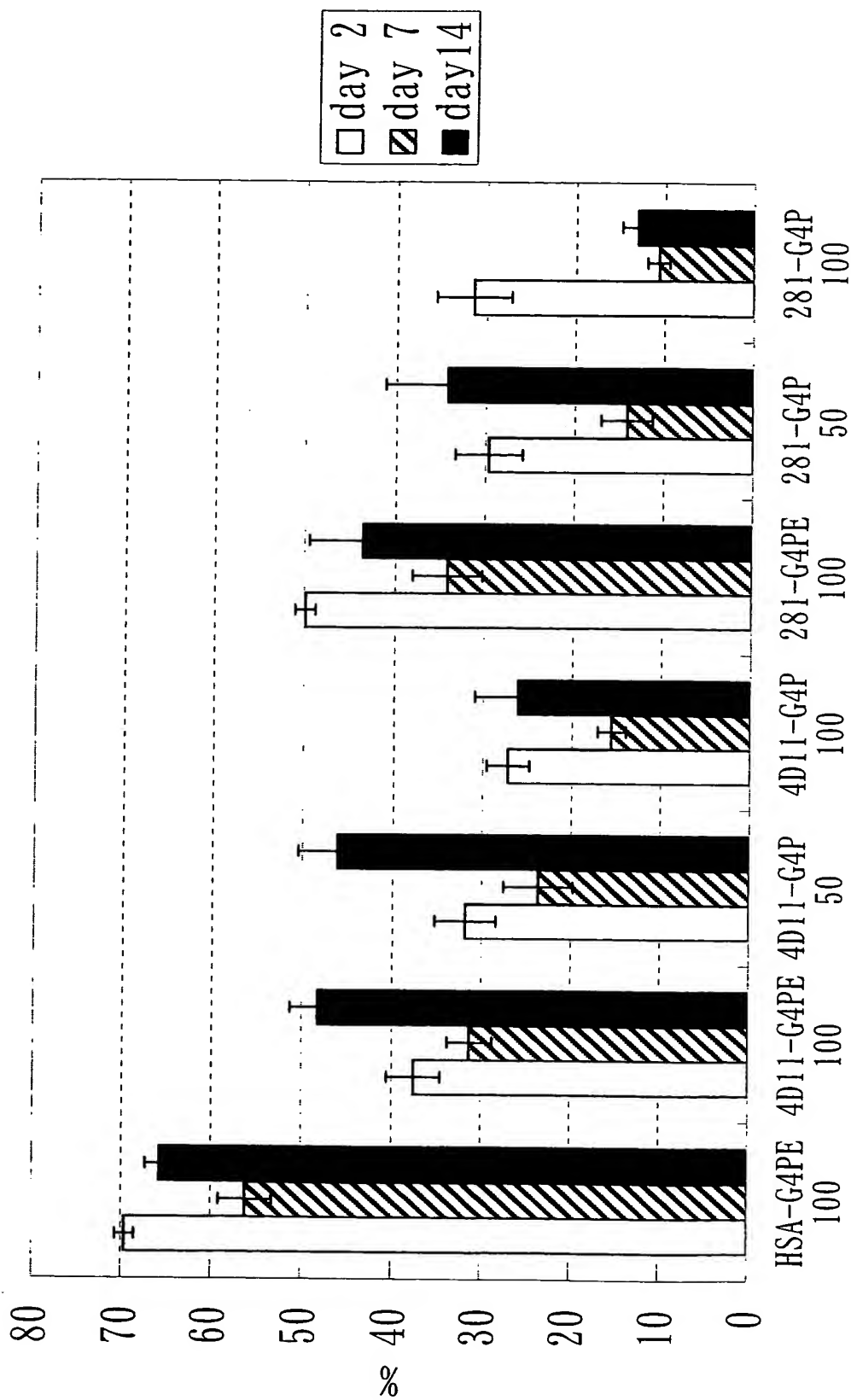




Fig. 14B

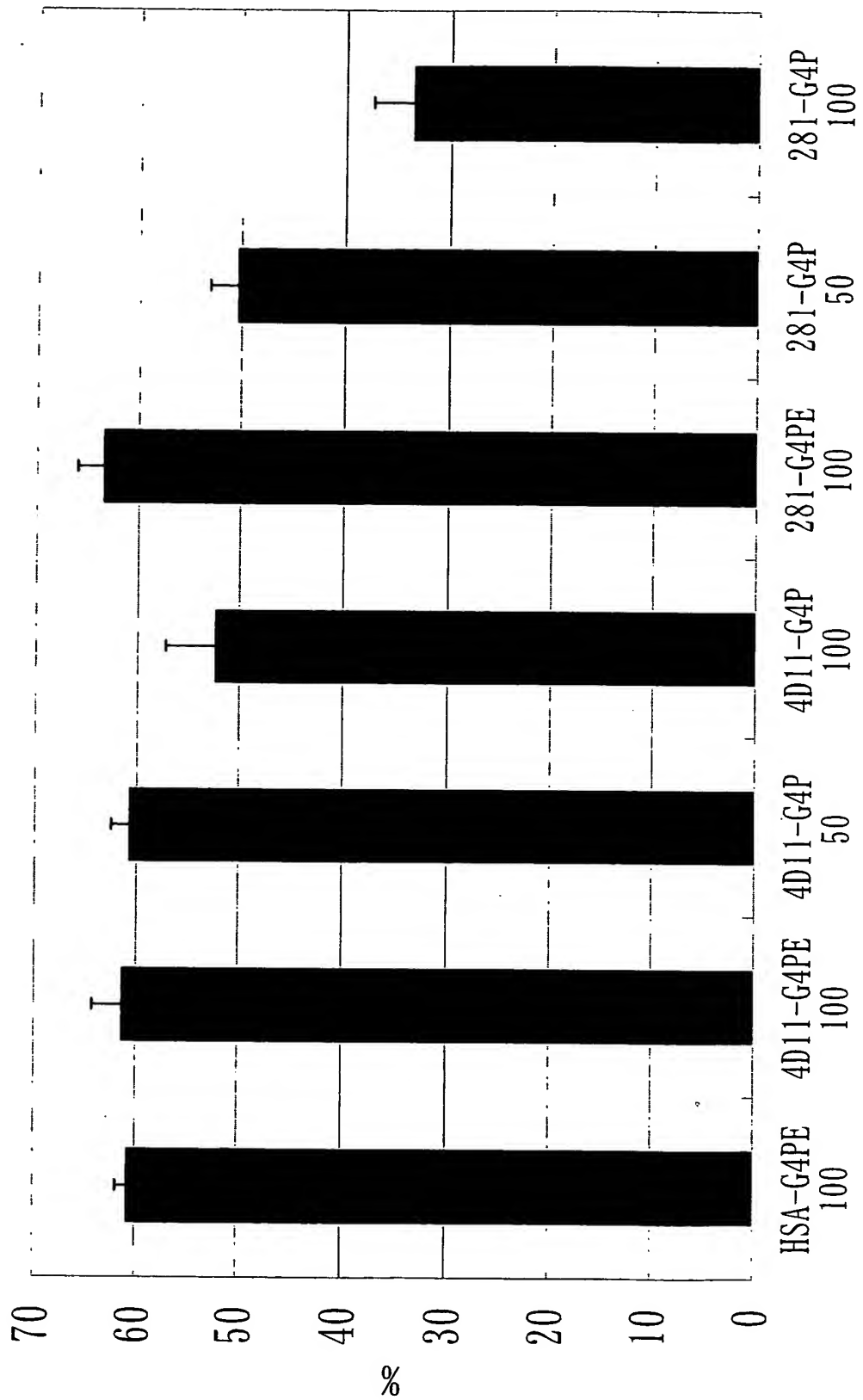


Fig. 15

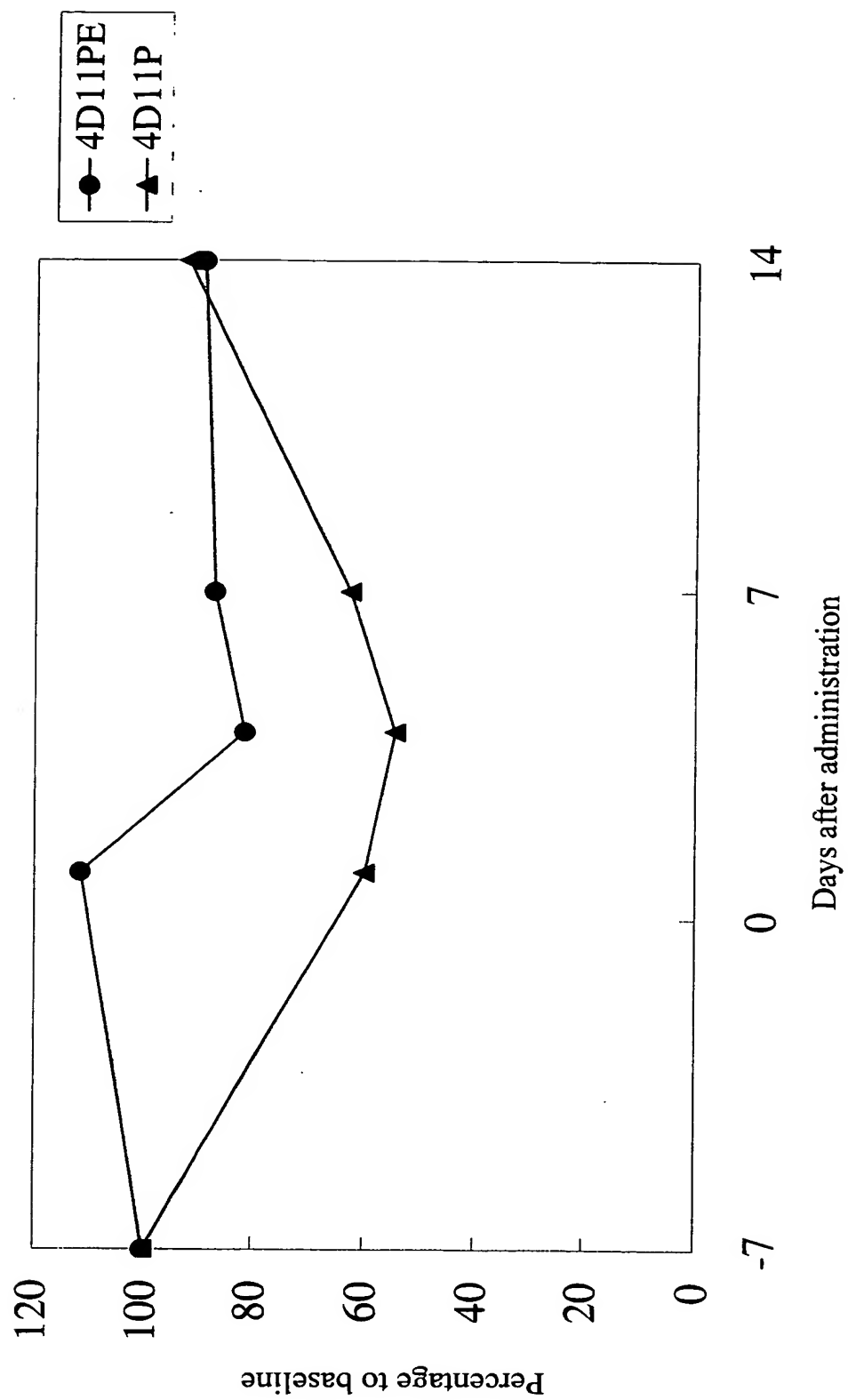


Fig. 16

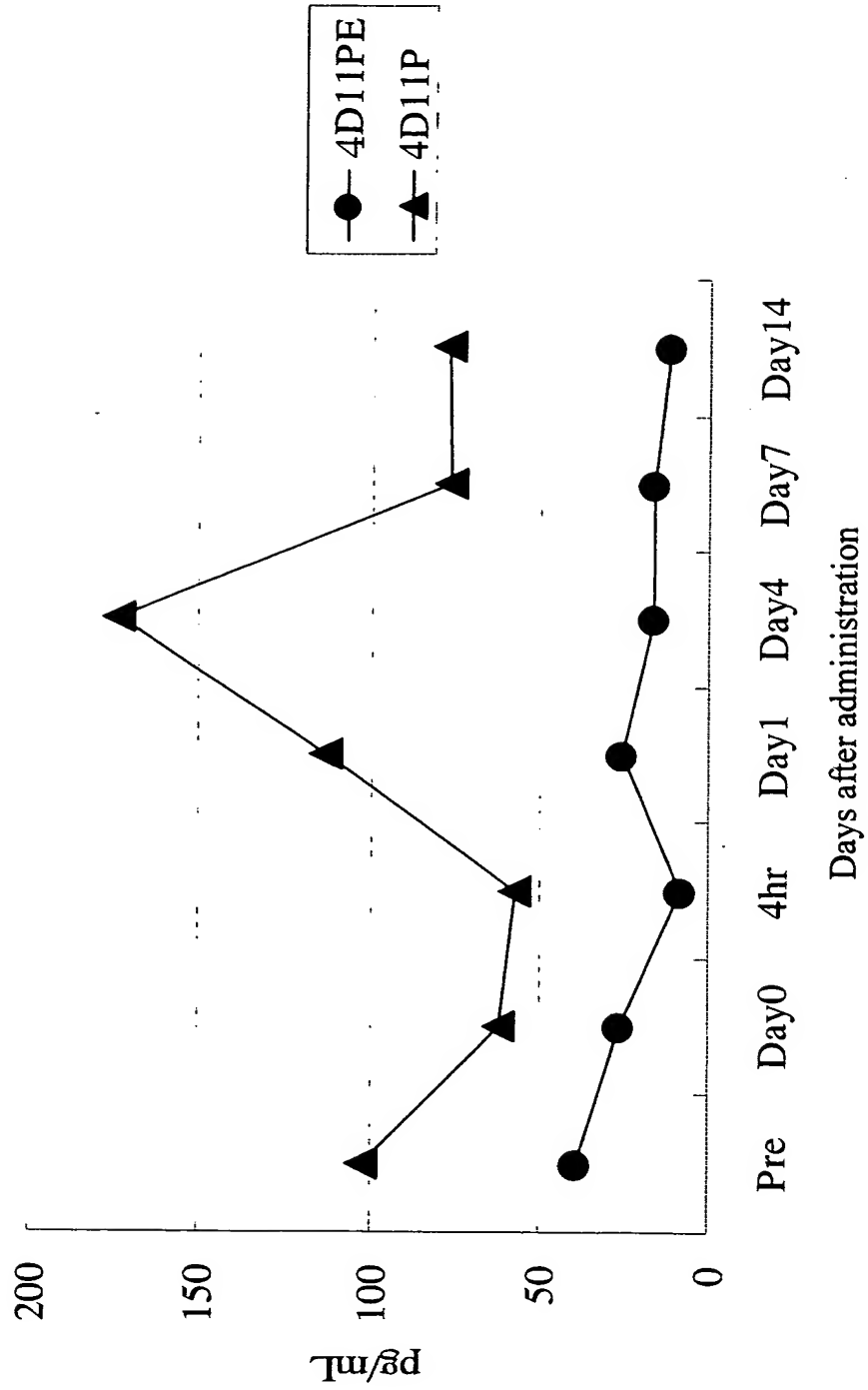


Fig. 17

Treatment		Average score*	
Group (mg/kg)	Tetanus toxoid Sensitization Dorsal intradermal Intramuscular challenge	24 hrs**	48 hrs**
Control	10 µL/site	0 Lf/mL	0.00
	x	1 Lf/mL	1.00
	12 sites	3 Lf/mL	2.67
		10 Lf/mL	3.00
4D11 1 (mg/kg)	10 µL/site	0 Lf/mL	0.00
	x	1 Lf/mL	0.67
	12 sites	3 Lf/mL	0.67
		10 Lf/mL	1.00
4D11 10 (mg/kg)	10 µL/site	0 Lf/mL	0.00
	x	1 Lf/mL	0.00
	12 sites	3 Lf/mL	0.33
		10 Lf/mL	0.67

* Response score	formation of erythema and/or eschar	formation of edema
no erythema	no erythema	no edema
very slight erythema (barely perceptible)	0	very slight edema (barely perceptible)
well-defined erythema	1	slight edema (edges of area well defined by definite raising)
moderate to severe erythema	2	moderate edema (raised about 1 mm)
from severe erythema to slight crust (deep injury)	3	severe edema (raised 1 mm or more and extending beyond area of exposure)
** time after challenge	4	

Fig. 18

Group	Animal No.	pre	(Maximum dilution rate for positive effect)							
			Days after the 1st dose							
			4	7	11	14	18	21	23	
Control	1	0	200	0	12800	102400	204800	204800	204800	
	2	0	0	0	6400	25600	51200	51200	51200	
	3	0	0	0	6400	12800	25600	25600	25600	
	Mean	0	67	0	8533	46933	93867	93867	93867	
	S.D.	0	115	0	3695	48460	96920	96920	96920	
1 (mg/kg)	4	0	0	0	200	1600	12800	12800	12800	
	5	0	0	0	200	400	6400	6400	6400	
	6	0	0	0	400	3200	6400	6400	6400	
	Mean	0	0	0	267	1733	8533	8533	8533	
	S.D.	0	0	0	115	1405	3695	3695	3695	
10 (mg/kg)	7	0	0	0	0	0	0	0	0	
	8	0	0	0	0	0	0	0	0	
	9	0	0	0	0	0	0	0	0	
	Mean	0	0	0	0	0	0	0	0	
	S.D.	0	0	0	0	0	0	0	0	

Fig. 19

Group	Animal No.	pre	Days after the 1st dose							(Maximum dilution rate for positive effect)
			4	7	11	14	18	21	23	
Control	1	0	0	0	3200	6400	6400	6400	6400	6400
	2	0	0	0	1600	1600	1600	1600	1600	800
	3	0	0	0	800	1600	1600	1600	1600	1600
	Mean	0	0	0	1867	3200	3200	3200	3200	2933
	S.D.	0	0	0	1222	2771	2771	2771	2771	3029
1 (mg/kg)	4	0	0	0	0	0	400	0	0	0
	5	0	0	0	0	0	0	0	0	0
	6	0	0	0	0	800	800	800	800	800
	Mean	0	0	0	0	267	400	267	267	267
	S.D.	0	0	0	0	462	400	462	462	462
10 (mg/kg)	7	0	0	0	0	0	0	0	0	0
	8	0	0	0	0	0	0	0	0	0
	9	0	0	0	0	0	0	0	0	0
	Mean	0	0	0	0	0	0	0	0	0
	S.D.	0	0	0	0	0	0	0	0	0

Fig. 20A

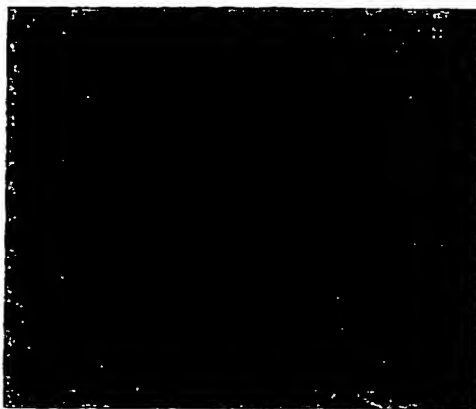
Human control IgG4



Anti-CD40 antibody (4D11)



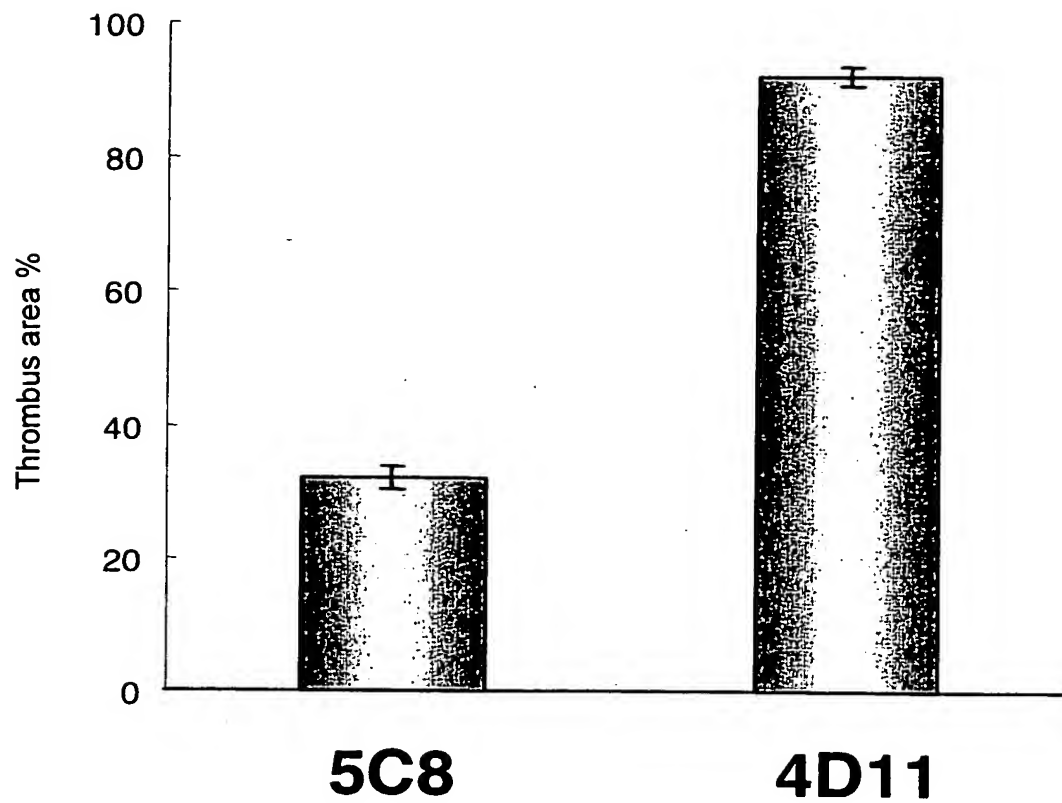
Murine control IgG2



Anti-CD40L antibody (5C8)



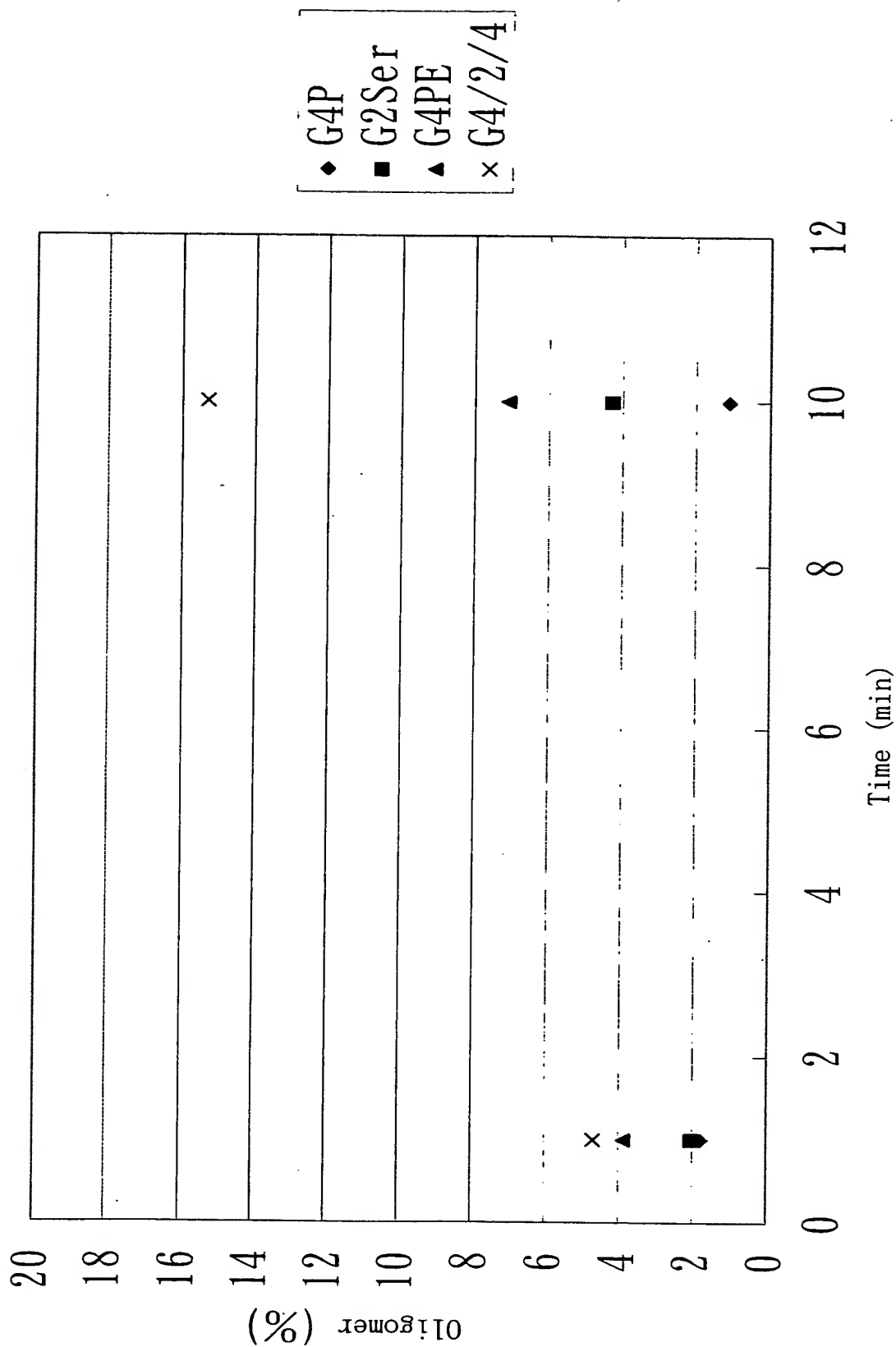
Fig. 20B



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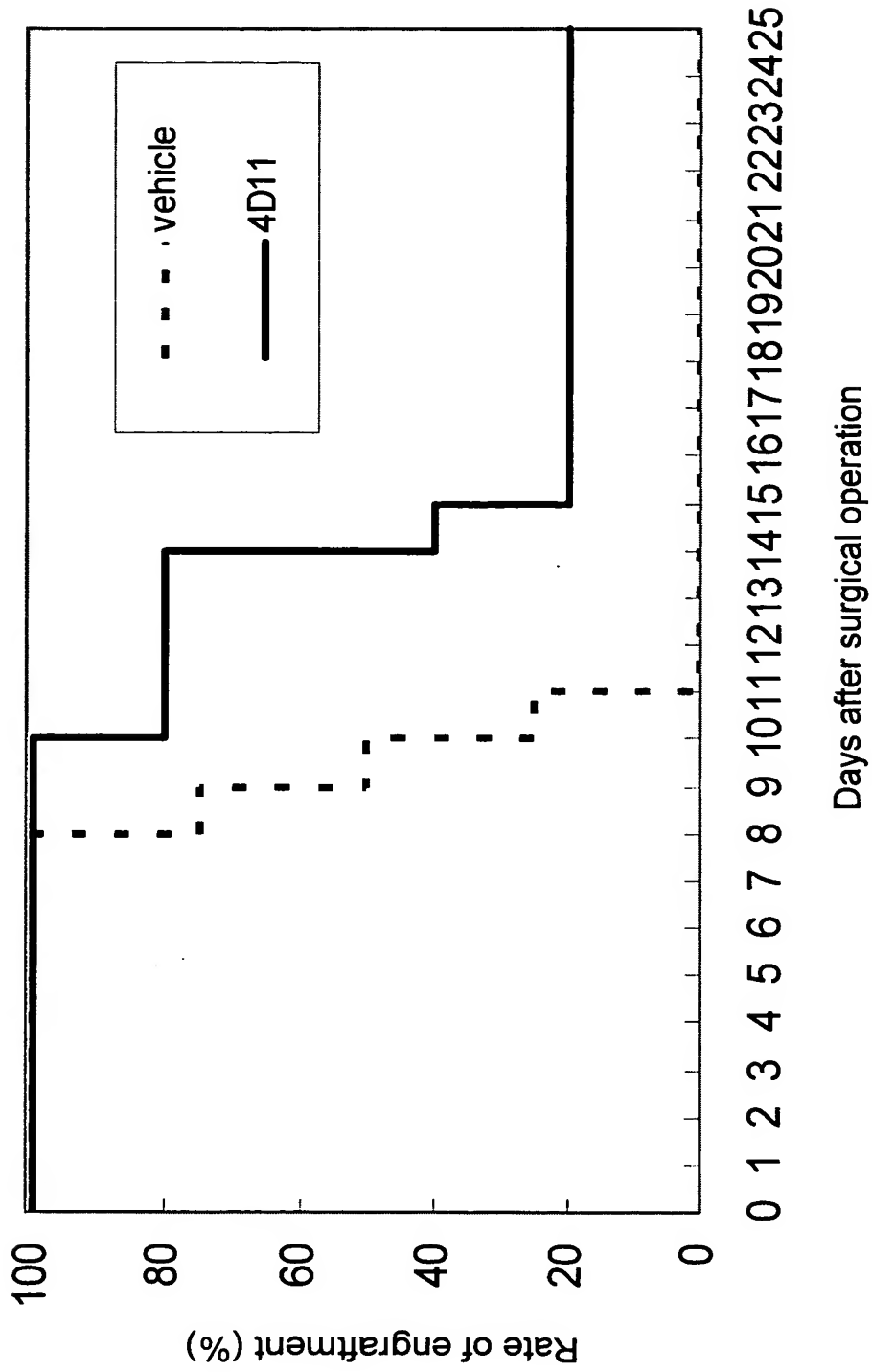


Fig. 21



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Fig. 22



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Fig. 23

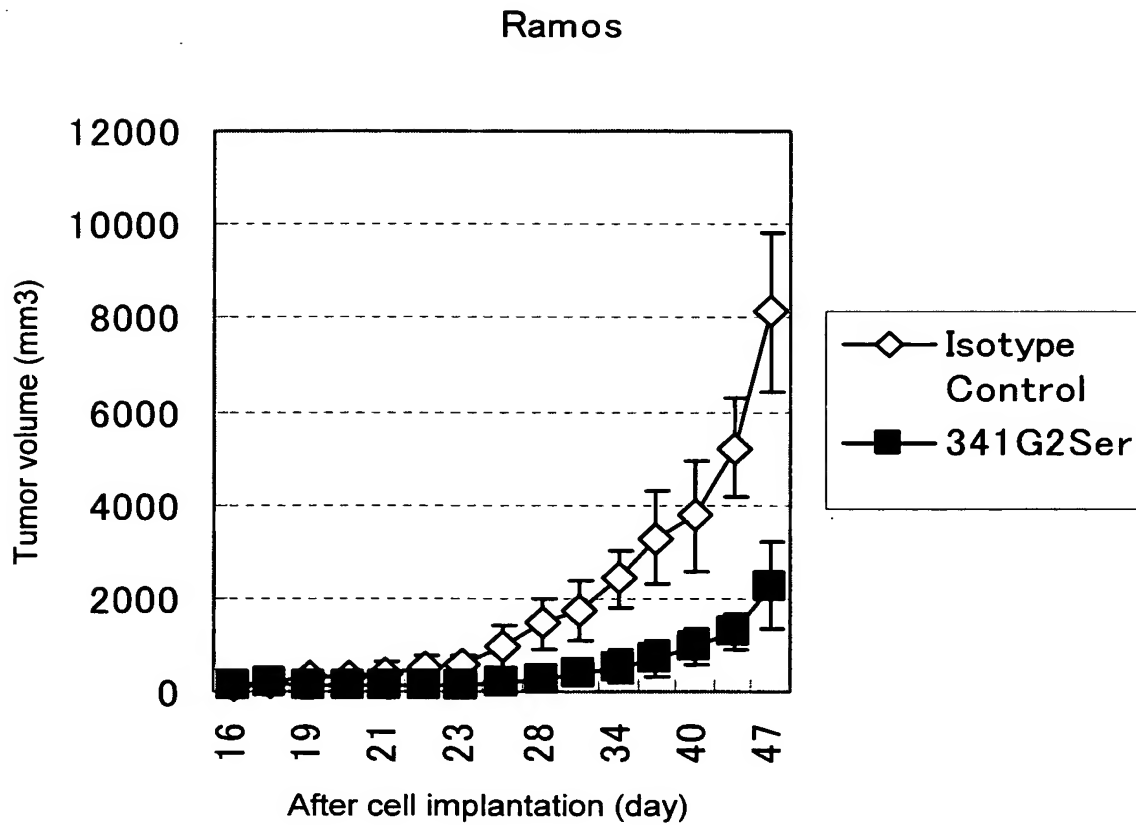


Fig. 24

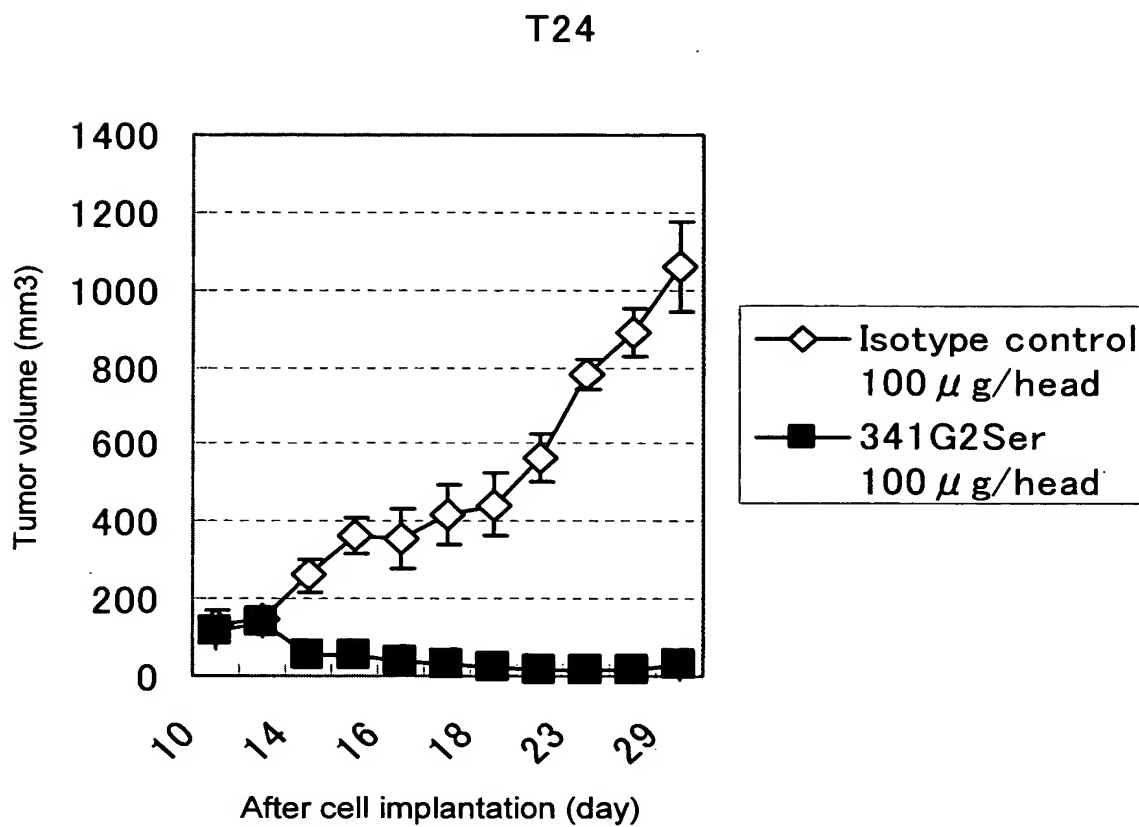


Fig. 25

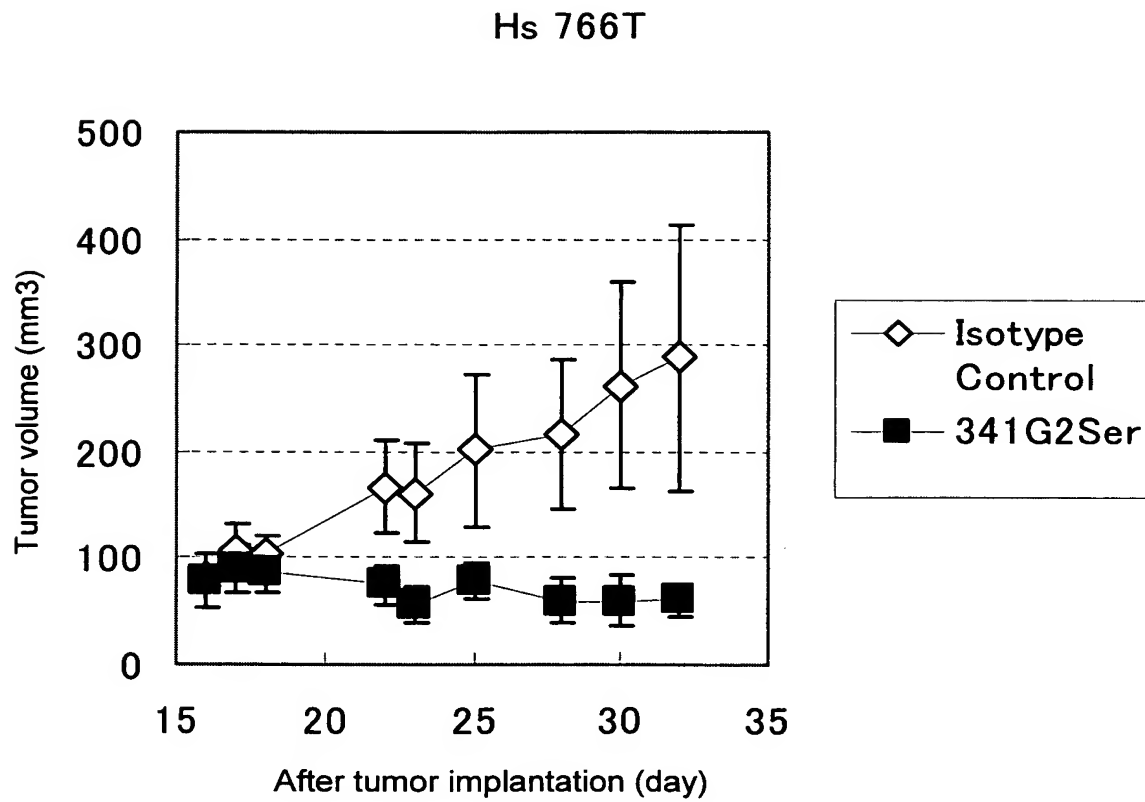
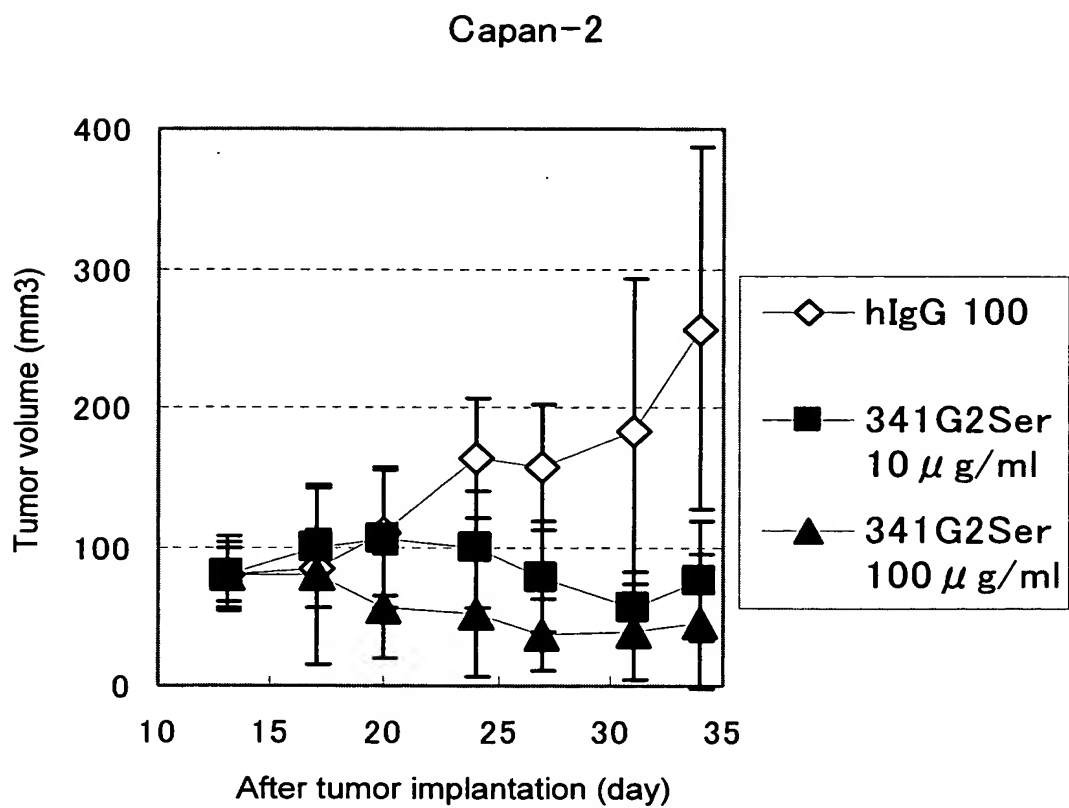


Fig. 26



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